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VOLUME XXII NUMBER 3

DISEASES

of the

CHEST

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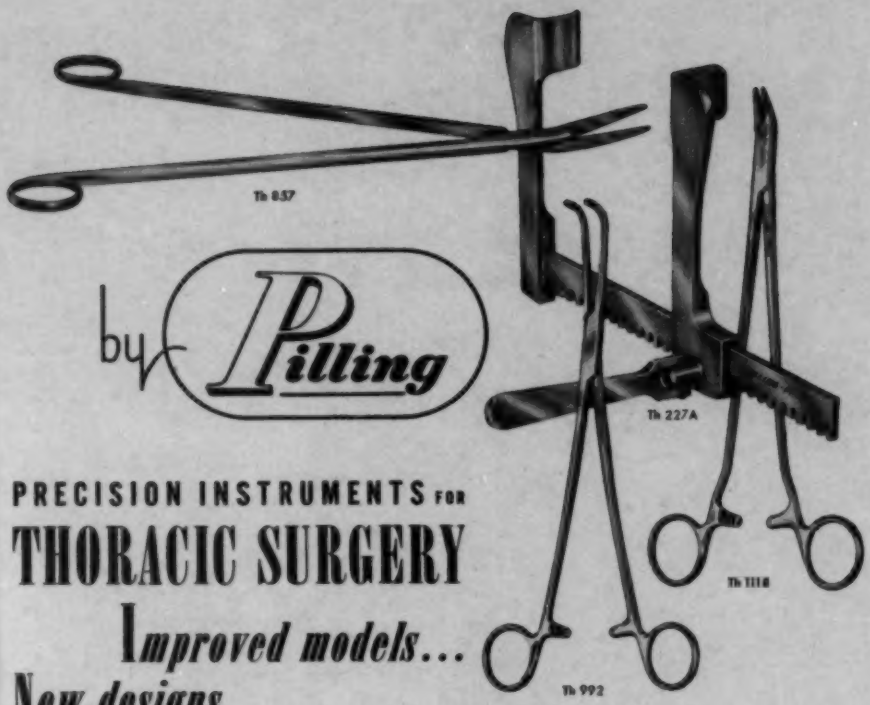

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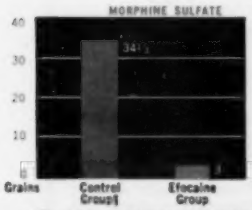

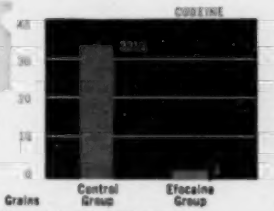

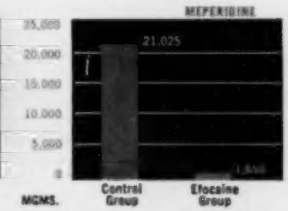

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LITERATURE ON REQUEST

Steere, A. H., and Shubat, E. L.: A New Approach to the Problem of Postoperative Pain, Am. J. Surg. 88, (April) 1954.

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DISEASES *of the* CHEST

OFFICIAL PUBLICATION

OF THE

AMERICAN COLLEGE OF CHEST PHYSICIANS

EXECUTIVE OFFICE
112 East Chestnut Street, Chicago 11, Illinois
MURRAY KORNFELD, *Managing Editor*

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CONTENTS:

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NEBULIZATION of Tryptar by standard aerosol technique marks a NEW ADVANCE in the management of respiratory disorders associated with hypersecretion and accumulation of fibrinomucinous material.

(Limber, C. R.; Reiser, H. G.; Roettig, L. C., and Curtis, G. M.: Enzymatic Lysis of Respiratory Secretions by Aerosol Trypsin, J.A.M.A. 149: 816-821, (June 28) 1952.

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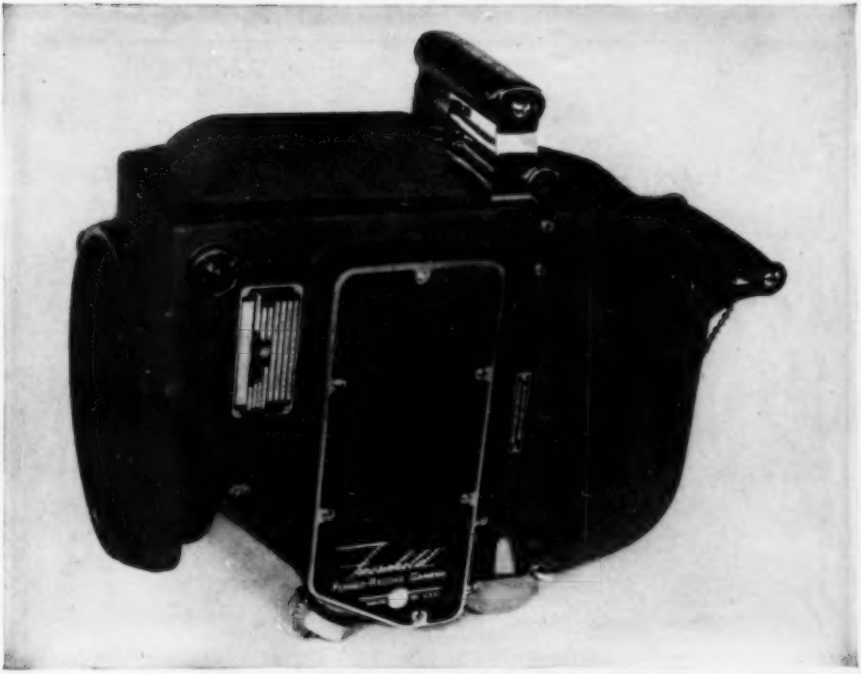

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1. Dixler, M.: Dosage and Blood Levels of Para-Aminosalicylic Acid, Schweiz. Ztschr. Tuberk. 7:6 (1950).

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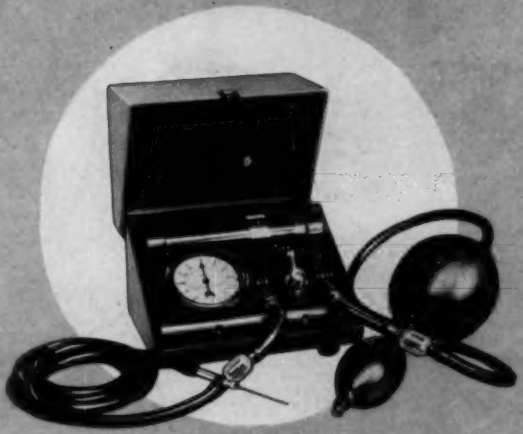

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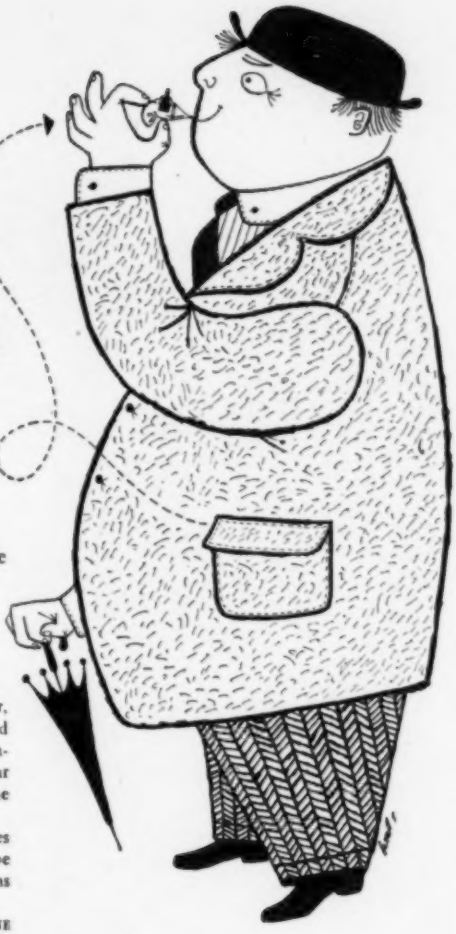

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1. Kaufman, R., and Farmer, L. (1951), Norisodrine by Aerohalor in Asthma, Ann. Allergy, 9:99, January-February.
2. Swartz, H. (1950), Norisodrine Sulphate (25 Per Cent) Dust Inhalation in Severe Asthma, Ann. Allergy, 8:488, July-August.
3. Krasno, L., Grossman, M., and Ivy, A. (1949), The Inhalation of 1-(3',4'-Dihydroxyphenyl)-2-Isopropylaminoethanol (Norisodrine Sulfate Dust), J. Allergy, 20:111, March.

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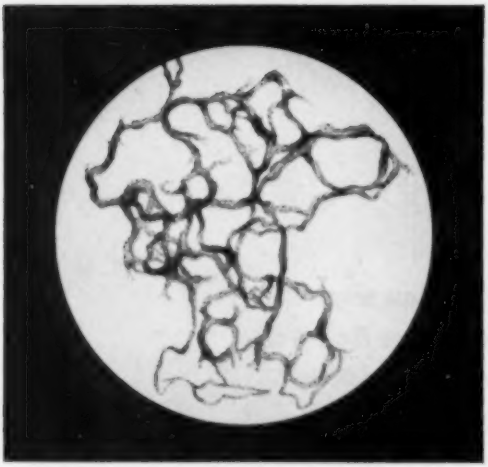
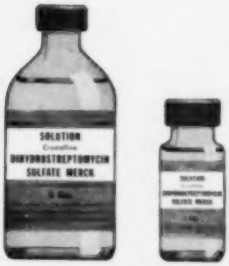


Serpentine growth characteristic of virulent human strains



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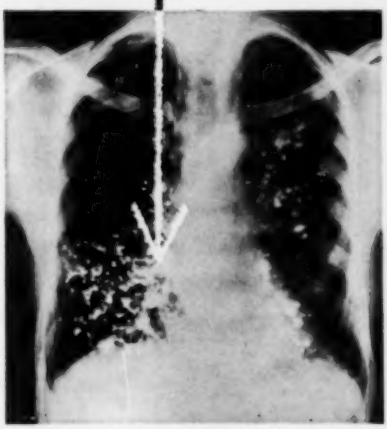

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1. Yater, W. M.: Fundamentals of Internal Medicine, ed. 3, New York, Appleton-Century-Crofts, 1949, p. 315.
2. Myers, J. A., and McKinlay, C. A.: The Chest and the Heart, Springfield, Ill., Charles C Thomas, 1948, p. 307.
3. White, B. V., and Geschickter, C. F.: Diagnosis in Daily Practice, Philadelphia, J. B. Lippincott Co., 1947, p. 419

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DISEASES *of the* CHEST

VOLUME XXII SEPTEMBER 1952 NUMBER 3

Hypothermia as a Means of Performing Intracardiac Surgery Under Direct Vision*

BRIAN A. COOKSON, M.B., Ch.B., (Edin.), WILFORD B. NEPTUNE, M.D. and CHARLES P. BAILEY, M.D., F.C.C.P.
Philadelphia, Pennsylvania

One of the aims of cardiac surgery today is to discover an innocuous method of rendering the chambers of the heart bloodless, so that they may be opened to permit definitive operations on the valves and septa under direct vision. It is felt by most investigators that the best way to achieve this is to allow the blood to by-pass the heart and lungs and flow through a mechanical heart and an artificial oxygenator. However, in hypothermia the possibility of a much more simple method exists.

Bigelow and his associates[1] demonstrated that when a dog's body temperature is dropped from 38 degrees C. (100 degrees F.) to 20 degrees C. (68 degrees F.) metabolism and the oxygen demands of the body are reduced approximately to 18 per cent of their normal value. They further demonstrated that hypothermia, provided it is suitably induced and does not go lower than 20 degrees C., is a comparatively safe procedure. A markedly reduced metabolism at 20 degrees C. suggested to them that the circulation could be safely stopped for a far longer period of time than is possible at normal temperature.[2,3] In order to check this, they demonstrated that dogs can survive occlusion of both the superior and inferior venae cavae for at least 15 minutes without brain damage. Furthermore they showed that cardiotomy of the left auricle could be performed with survival under these conditions.

*From the Experimental Surgical Laboratory of the Division of Surgery, Department of Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania.

This work was supported by U.S.P.H. Grant H-394, and The Mary Bailey Foundation.

Unfortunately, the percentage of survival in 39 such experiments was only 15 per cent. Forty-nine per cent died due to either ventricular fibrillation or cardiac arrest during occlusion of the cavae or shortly after caval occlusion was relieved. Of the animals revived to normal temperature, 70 per cent died of shock within 12 hours.

Stimulated by these experiments, we decided to repeat the work of these investigators in the hope that by making various modi-

TABLE I

CARDIOTOMY OF RIGHT VENTRICLE

Series No.	Type	Date	Comments	Survival
1F	Caval occlusion 12 minutes R. T. 25° C.	21 Jan. 1952		Yes
2F	Caval occlusion 12 minutes R. T. 26° C.	23 Jan. 1952	Inequality of pupils, otherwise normal.	Yes
3F	Caval occlusion 12 minutes R. T. 25.5° C.	25 Jan. 1952		Yes
4F	Caval occlusion 12 minutes R. T. 26° C.	28 Jan. 1952	Dog made very slow postoperative recovery. No obvious CNS damage. Dog not very cooperative.	Yes
5F	Caval occlusion 12 minutes R. T. 25.5° C.	29 Jan. 1952	Inequality of pupils, otherwise normal.	Yes
6F	Caval occlusion 12 minutes R. T. 24° C.	30 Jan. 1952		Yes
7F	Caval occlusion 12 minutes R. T. 26° C.	31 Jan. 1952	*Severe Heart block* Effective circulation reestablished late. Survived 21 hours.	No
8F	Caval occlusion 12 minutes R. T. 26° C.	4 Feb. 1952	Animal in good condition until pressure pneumothorax developed. Slow recovery. Definite cerebral lesion.	Yes
9F	Caval occlusion 12 minutes R. T. 26° C.	5 Feb. 1952		Yes
10F	Caval occlusion 12 minutes R. T. 25° C.	6 Feb. 1952	*Cardiac arrest* followed by ventricular fibrillation.	No
11F	Caval occlusion 12 minutes R. T. 26° C.	13 Feb. 1952		Yes

fications we might eliminate the problems they had encountered and hence achieve a more satisfactory recovery rate.

After 10 preliminary experiments we evolved a standard procedure which enabled us to occlude the cavae for 12 minutes and perform cardiotomy on the right ventricle in 11 consecutive dogs with 9 survivals (Table I).

Technic

A non-fasting dog is premedicated with morphine sulfate, 1 mgm./kgm., and atropine sulfate, .04-.08 mgm./kg., intraperitoneally. Thirty minutes later the dog is anesthetized with 30 mgm./kg. of sodium pentothal, intravenously. An endotracheal tube is then inserted and a needle for intravenous therapy is placed in one of the veins of the right front leg. The animal is placed on its left side in a cold chamber* with air circulating by means of a fan at approximately minus four degrees C. (25 degrees F.). Padding is provided to prevent contact with cold metal. Respiration is controlled by means of a pneophore respirator† supplying 100 per cent oxygen. The virtue of the pneophore respirator is that it can be used automatically either as a supply and demand system when the animal is breathing on its own or as an artificial respirator when breathing has ceased. In addition to these measures, the animal receives soluble penicillin, 1,000,000 Units, ACTH, 8 Wilson Units, and 50 per cent glucose intravenously, 1 cc./kg.

The animal is now periodically observed. Whenever shivering is seen, 50 mgm. of sodium pentothal is given intravenously. After 2½ to 3½ hours, the rectal temperature has usually dropped to 26 degrees C. (79 degrees F.). The animal is removed from the cold chamber and prepared for surgery.

The chest is opened through the fifth right intercostal space. Collapse of the lungs, to any degree, is scrupulously avoided by keeping them almost fully inflated and handling them gently. Immediately upon opening the chest, 10 cc. of 1 per cent Procaine Hydrochloride is injected into the pericardial sac. The azygos vein is then ligated and umbilical tapes are placed loosely about the superior and inferior venae cavae without occluding them. The pericardial sac is opened and the right ventricle is exposed. Four silk stay sutures are placed in the wall of the right ventricle to allow traction and control of the subsequent incision to be made in the wall of the ventricle.

The cavae are now occluded with vascular clamps and an incision is made in the wall of the right ventricle. The edges of the

*Victor Beverage Cooler.
†Obtained from the Mine Safety Appliance Co., Pittsburgh, Penna.

incision are retracted by pulling on the stay sutures enabling one to have an excellent view of the ventricular chamber. The small quantity of blood present is easily removed with either suction or gauze. The blood slowly reaccumulates as it trickles sluggishly out of the coronary sinus. Closure of the ventricular incision is quite rapid and simple. Two layers of silk sutures are used; the first layer consists of a continuous everting mattress suture, and the second layer of a continuous running whip-stitch.

After 12 minutes of caval occlusion, the superior vena cava is unclamped and Benodaine,§ 0.8 mgm./kg. (a short acting adrenolytic drug), is injected into the cavity of the right ventricle. The surgeon refrains from all intrathoracic manipulation and closely observes the heart, checking the rhythm and the rate. Five minutes after the removal of the superior vena caval clamp, the inferior vena cava is partially opened. After an additional five minutes, the dose of Benodaine is repeated and the inferior vena caval clamp is further opened. Finally, after another five minutes, the clamp is completely removed. The pericardial sac is resutured. A drainage tube, connected to water-seal suction, is left in the chest; the lungs are fully inflated and the chest is closed.

The animal is placed on a warming table and covered with an electric blanket. The dose of penicillin and glucose is repeated and 100 mgm. of Thiamine Hydrochloride is given intravenously. Re-warming to normal body temperature is arranged to take approximately three hours during which time 100 per cent oxygen is continuously supplied. When the animal shows signs of returning consciousness, which coincides approximately with the return to normal body temperature, the endotracheal and chest drainage tubes are removed, a final dose of glucose is given, the animal is placed in a comfortable place and left for the night. Next day the animal is given 200,000 Units depot Penicillin, and on the subsequent day is returned to the animal house.

The condition of the dog throughout the experiment is evaluated by a careful study of tongue color and reflexes. Ideally, immediately before caval occlusion, the tongue is bright red, the pupils are small and the conjunctival and deep tendon (knee) reflexes are present. At the end of 12 minutes of caval occlusion, the tongue is moderately anemic and cyanotic, the pupils are fully dilated and the reflexes are absent. The tongue becomes bright red again and the pupils return to their former size in 20 minutes after the release of the superior vena caval clamp. The conjunctival reflex is back in 45 minutes and the knee jerk in 60 minutes. A delayed return of reflexes is a bad prognostic sign.

§Benodaine is [2-(1-Piperidylmethyl) - 1,4 - Benzodioxan Hydrochloride Merck]. Supplied by Merck and Co., Inc., Rahway, New Jersey.

Results

In the 11 dogs in which this technic was used only one case of ventricular fibrillation was seen. This is in sharp contrast to Bigelow's results in which the reported incidence of ventricular fibrillation was as high as 36 per cent. (Bigelow's report does not enumerate those fibrillations which were successfully defibrillated). In our preliminary experiments, in which the adrenolytic drug Benodaine was not used, ventricular fibrillation commonly occurred after the caval occlusion was relieved (Table II).

The sequel of events without Benodaine was usually as follows: At the end of the period of occlusion, the heart was still beating weakly at a slow rate. Following the relief of the occlusion, the heart beat became rapid and vigorous, and shortly thereafter was converted into ventricular fibrillation. This typical picture was reminiscent of the effects of a large dose of Epinephrine.* It was then realized that during the occlusion of the cavae, due to anoxia, a discharge of Epinephrine from the adrenal medulla was pouring into the clamped off inferior vena cava. The fibrillation which followed the releasing of the clamps could therefore very likely be due to large quantities of accumulated Epinephrine reaching the anoxic heart. The fact that the use of Benodaine has almost eliminated this type of fibrillation lends strong support to this supposition. In fact the only dog which fibrillated (in the series of 11) was one which did not receive Benodaine until after the inferior vena cava was unclamped.

*We are indebted to Dr. Nicholas Dryer for this suggestion.

TABLE II

DATA FROM FOUR CONSECUTIVE EXPERIMENTS WITHOUT THE USE OF BENODAINE

Series	Rectal Temperature	Caval Occlusion	Method	Results
3B	20° C.	10 mins.	I.V.C. and S.V.C. simultaneously opened.	Immediate fibrillation.
4B	26° C.	12 mins.	I.V.C. and S.V.C. simultaneously opened.	Fibrillation 6 minutes later.
5B	23° C.	10 mins.	S.V.C. first unclamped. I.V.C. unclamped 6 minutes later.	Fibrillation 4½ minutes after removal of I.V.C. clamp.
6B	25° C.	9 mins.	S.V.C. first unclamped. I.V.C. clamp partially opened 10 minutes later and completely removed after another 5 minutes.	Fibrillation 5 minutes after complete removal of I.V.C. clamp.

The next significant fact is that only one out of the 10 dogs which survived surgery died postoperatively, whereas 70 per cent of Bigelow's surviving animals died of shock. It is well known that delayed death due to either pulmonery edema or shock frequently follows a prolonged interruption of the circulation. The occlusion of the cavae for only 12 instead of 15 minutes and the avoidance of ventricular fibrillation has no doubt given us an advantage in this respect.

In addition to this consideration, we took certain positive measures to combat shock and pulmonary edema:

1) The use of 50 per cent Glucose I.V.
2) Adequate ventilation with 100 per cent oxygen during the entire period of unconsciousness.
3) The use of sedative premedication to reduce the dose of pentothal necessary for anesthesia.
4) The avoidance of pulmonary collapse and pneumothorax by:
   (a) Avoiding use of animals with obvious respiratory infections.
   (b) Adequate Atropine premedication to prevent the unusually copious bronchial secretions normally occurring during hypothermia.

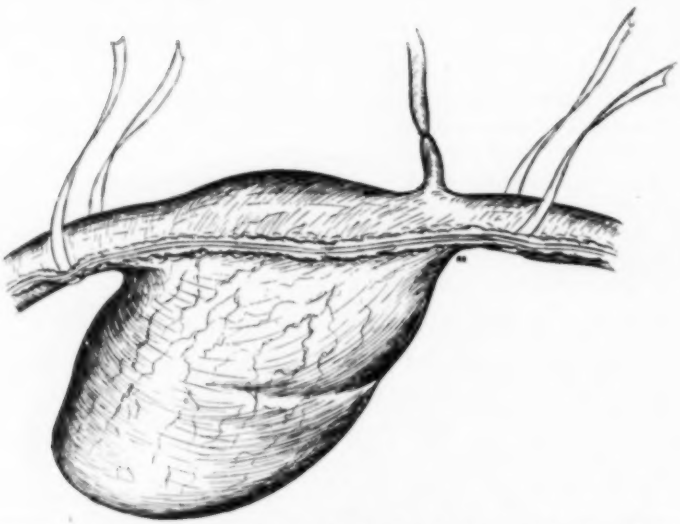

FIGURE 1: Diagramatic drawing of the heart showing ligation of the azygos vein, umbilical tapes round the superior and inferior venae cavae, with the pericardium still intact.

(c) Operating with lungs almost fully inflated.
(d) Leaving a drainage tube in the chest.

5) Avoidance of infection by: (a) liberal doses of penicillin prophylactically, (b) rules of asepsis.
6) Routinely insuring against Thiamine deficiency.
7) The use of ACTH.

Possibly the use of the adrenolytic drug Benodaine should be included on this list, although it was not intentionally used for this purpose.

The two deaths (the one postoperatively and the other during surgery) experienced in this series of 11 dogs were due primarily in the one case to severe heart block following 12 minutes of caval occlusion and the other to cardiac arrest, which also followed caval occlusion. In the first animal, no attempt was made to relieve the heart block for a period of 30 minutes. The ventricles were contracting weakly at an average rate of 20/minute (normal rate at 26 degrees C. is 60/minute). Finally cardiac massage was carried out and the heart block disappeared and the ventricles beat forcefully at a rate of 48/minute. This animal died 21 hours later of shock. There is no doubt that the administration of Benodaine helped only to accentuate the heart block. The logical procedure would have been to give the heart a small dose of Epinephrine. This was tried in the case of the animal with cardiac arrest: Benodaine was withheld and the animal's own Epinephrine was administered by opening the inferior vena caval clamp. Once the heart had resumed its beat, Benodaine was given. Unfortunately this heart fibrillated and we were not able to defibrillate it successfully.

Of the 9 survivors in this series, one dog showed signs of gross neurological damage. On the seventh postoperative day, this dog walked in clockwise circles with a stamping gait and bumped into objects as if blind. In another week these symptoms were much ameliorated and the dog was quite responsive. Another dog showed behaviour which was suspicious of transient neurological damage. This animal did not attempt to walk until 72 hours after surgery (the majority of animals walked within 24 hours); but, apart from very great weakness, the gait was normal. In two more days the animal, aside from being lazy and not very responsive, behaved like a normal dog. Both of these animals were febrile (40 degrees C., normal temperature 38 degrees C.) for the first 24 hours after surgery, and the possibility of distemper cannot be absolutely ruled out. All the remaining animals appeared normal in every respect except for an additional two dogs which showed a transient inequality of the pupils postoperatively.

FIGURE 2: Drawing to show the vascular clamps used to occlude the cavae. The pericardium has been opened and the stay-sutures are placed in the auricle for control of the subsequent incision.

Subsequent Experiments

After five more experiments, a modified standard procedure was evolved mainly designed to eliminate the problems of cardiac arrest, heart block and neurological damage. With this modified procedure, and with an average of 12 minutes caval occlusion as before, a series of 8 cardiotomies were performed on the right ventricle with one death (Table III); and eight cardiotomies on the right auricle with one death (Table IV). Both deaths occurred many hours after surgery. One was due to gross hemorrhage and the other was unexplained except that the operation was complicated by damage to a small portion of lung which had to be repaired. No neurological damage was seen in any of the survivors. The following improvements and modifications of technic were made.

First, it was found that the dose of Pentothal could be decreased if the premedication dose of Morphine and Atropine was given subcutaneously instead of intraperitoneally. Second, it was decided that it was more logical to give Thiamine at the beginning of hypothermia rather than after surgery. Third, it was noted that hypothermic dogs had a better circulation if digitoxin, 0.014 mgm./kg., intravenously, was given at the beginning of the ex-

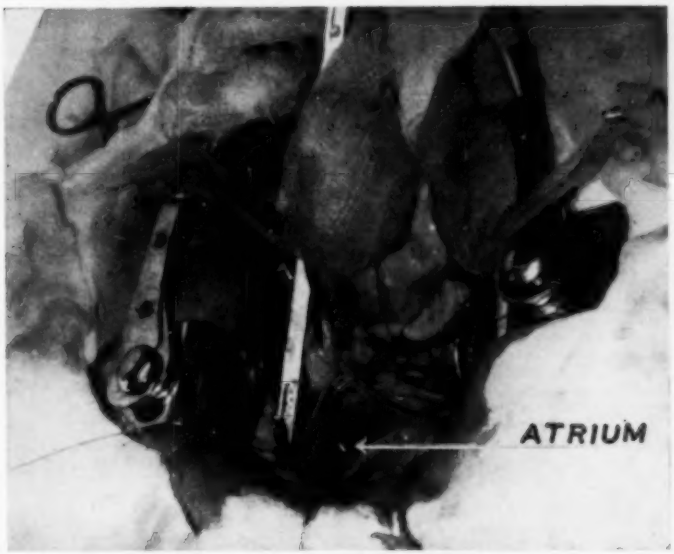

FIGURE 3: Photograph of a dog's heart showing the opened right auricular chamber.

periment. Fourth, an additional dose of Glucose was given just prior to the chest being opened. Fifth, throughout surgery the blood pressure was maintained by small doses of Vasoxyl, intravenously. Sixth, in cases where a marked bradycardia occurred, during the induction of hypothermia, an additional dose of Atropine was given.

If the above measures are employed, it is found that the heart is still beating strongly at the end of the period of caval occlusion. After the superior vena cava is unclamped, Benodaine is withheld until it is ascertained that the heart is beating satisfactorily (i.e. 32/minute or more) and is showing no signs of heart block.

TABLE III

ADDITIONAL SERIES OF RIGHT VENTRICULAR CARDIOTOMIES

Series No.	Type	Date	Comments	Survival
1K	Caval occlusion 15 minutes R. T. 22° C.	29 Feb. 1952		Yes
2K	Caval occlusion 12 minutes R. T. 26° C.	5 Mar. 1952	Animal bad operative risk. Pneumonia. Middle lobe of right lung consolidated.	Yes
3K	Caval occlusion 10 minutes R. T. 27° C.	6 Mar. 1952	*Cardiac arrest* at end of occlusion period. Animal received too much pentothal during induction.	Yes
4K	Caval occlusion 12 minutes R. T. 25.5° C.	3 May 1952	*Fibrillation* when ventricle incised.	Yes
5K	Caval occlusion 12 minutes R. T. 23° C.	6 May 1952	*Fibrillation* during manipulation of heart. Late death due to severe hemorrhage.	No
6K	Caval occlusion 12 mins. 2 papillary muscles cut & repaired. R. T. 25° C.	15 May 1952	*Fibrillation* when ventricle incised.	Yes
7K	Caval occlusion 13 mins. Continuous incision involving right ventricle and pul. art. R. T. 22.5° C.	20 May 1952	*Fibrillation* during manipulation of heart.	Yes
8K	Caval occlusion 10 mins. One papillary muscle cut & repaired. R. T. 24.5° C.	27 May 1952	*Fibrillation* when ventricle incised.	Yes

The dose of Benodaine is 0.6 mgm./kg. One and one half minutes after giving Benodaine, the inferior vena caval clamp is half opened. Two to three minutes later the inferior vena caval clamp is completely removed. The heart is then watched for 10 minutes after which time the pericardial sac is closed and the operation completed.

If a diagnosis of heart block or unsatisfactory rate (i.e. less than 32/minute) is made, it should be made not earlier or later than two minutes after the superior vena caval clamp is removed. One cc. of fresh 1:4000 Epinephrine, prepared in advance, should be immediately injected into the right ventricle and the heart gently massaged. If the heart does not respond in one and one half minutes, the heart is continuously massaged for five minutes or more and the inferior vena caval clamp removed. Usually, however, the heart promptly responds in which case once the heart beat is well established (i.e. 40/minute) Benodaine is given and the opening of the inferior vena caval clamp is commenced one minute later.

Ventricular fibrillation is a frequent complication of the treat-

TABLE IV
RIGHT AURICULAR CARDIOTOMY

Series No.	Type	Date	Comments	Survival
1J	Caval occlusion 12 minutes R. T. 27° C.	27 Mar. 1952		Yes
2J	Caval occlusion 13 minutes R. T. 26° C.	4 Apr. 1952		Yes
3J	Caval occlusion 12 minutes R. T. 26° C.	22 Apr. 1952	*Fibrillation* during manipulation of heart.	Yes
4J	Caval occlusion 12 minutes R. T. 23° C.	9 May 1952		Yes
5J	Caval occlusion 12 minutes R. T. 25° C.	21 May 1952	Cause of death unknown. Lung was injured.	No
6J	Caval occlusion 12 minutes R. T. 26° C.	22 May 1952		Yes
7J	Caval occlusion 12 minutes R. T. 26.5° C.	26 May 1952		Yes
8J	Caval occlusion 11 minutes R. T. 24.5° C.	28 May 1952	*Fibrillation* during cardiotomy.	Yes

ment of cardiac arrest with Epinephrine. It also frequently occurs in the hot humid summer months when the ventricles are handled or incised. This latter type of fibrillation was not observed in the winter months. No difficulty is experienced in defibrillating these hearts provided it is done immediately. In an efficient team, less than 30 seconds should elapse between the onset of fibrillation and the application of an electric shock to the ventricles. If the heart is not defibrillated in two attempts, 1 cc. of 1:4000 Epinephrine is injected into the left ventricle, the heart is vigorously and effectively massaged for one minute and electric shock is again tried.

This emphasis on light anesthesia, improved circulation, and rapid recovery of circulation has resulted in a much faster return of reflexes. The knee jerk has often returned within 30 to 40 minutes after the removal of the superior vena caval clamp. The animals experience far less shock. It has been possible with this technic to operate on a dog which is a bad operative risk, such as an animal with pneumonia.

Having improved the technic for caval occlusion at 26 degrees C. for 12 minutes, we wished to work at lower temperatures for longer periods of time. In our non-surgical experiments on hypothermia alone, we had noted that below 20 degrees C. the heart suddenly changed its rhythm and became very slow, dropping from an average rate of 30/minute to five or 6/minute. This was usually, but not invariably concomitant with a change from sinus to nodal rhythm. Shortly after this the tongue became paler and the pulse weak or impalpable. This common occurrence discouraged us from performing any surgery at these temperatures. However, quite by chance we discovered that if 100 mgms. of WIN 2173 was injected I.V., the heart would revert back to its normal rate of 30/minute and the pulse would again become palpable.[4] This effect would last 30 to 45 minutes when another dose became necessary. Making use of this discovery, we operated on five dogs at 17 degrees C. (Table V), occluding the cavae in each case for 30 minutes and opening the right auricle for approximately 20 minutes. Two animals survived this treatment and were perfectly normal. One animal was killed accidentally and two dogs died of ventricular fibrillation. These were preliminary experiments, but it was felt that, if necessary, a survival rate similar to that reported above could be obtained with perserverance. The most encouraging fact is that in each instance the heart kept beating throughout the 30 minutes of caval occlusion. It was also interesting to note that the pupils did not dilate at this temperature.

We also realized that hypothermia would give us sufficient time to remove a dog's heart and lungs and substitute those of another

dog. Such a procedure was done, successfully, in three experiments. Both donor and recipient dogs were cooled to 24 degrees C. and a technic devised whereby the substitution could be made in less than 15 minutes. In the most successful of three such experiments, which are to be reported elsewhere,[5] the animal survived for six hours after the substitution with a normal electrocardiogram (i.e. for 24 degrees C.) and return of reflexes and spontaneous respiration.

Discussion

In view of these highly encouraging results, it is justifiable to consider the feasability of performing cardiac surgery on humans under hypothermia. For several reasons hypothermia seems unusually well suited to the problem of congenital heart disease in infants. First, the majority of congenital lesions can be approached from the right side of the heart. Second, infant mammals are much less sensitive to hypothermia and asphyxia than more mature animals.[6] Third, infants, being small, can more readily be cooled and rewarmed.

It would be logical to begin with humans cooled to 26 degrees C. (79 degrees F.) as there are several instances on record of humans tolerating this temperature.[7-11] In most of the observations made on man, it is reported that auricular fibrillation frequently occurs at this temperature.[10] The cases were not, however, artificially respired with oxygen and were only lightly sedated. Heavier sedation and ventilation with 100 per cent oxygen may well prevent the occurrence of auricular fibrillation or arhythmias.

TABLE V

RIGHT AURICULAR CARDIOTOMY WITH PROLONGED CAVAL OCCLUSION AT 17° C.

Series No.	Type	Date	Comments	Survival
1M	Caval occlusion 30 minutes R. T. 17° C.	25 Apr. 1952	Killed accidentally	No
2M	Caval occlusion 30 minutes R. T. 15.5° C.	1 May 1952	*Fibrillation* 10 minutes after chest closed.	No
3M	Caval occlusion 30 minutes R. T. 16° C.	7 May 1952		Yes
4M	Caval occlusion 30 minutes R. T. 17° C.	12 May 1952	*Fibrillation* during terminal part of cardiotomy.	Yes
5M	Caval occlusion 30 minutes R. T. 17° C.	17 May 1952		Yes

The hardest question to answer is how long we might safely occlude the cavae in hypothermic humans? In finding an answer to this question various facts should be considered. It is the consensus of opinion that an adult man can usually survive, without harm, a maximum of three to four minutes of absolute circulatory arrest at normal body temperature. Caval occlusion is not, however, the same thing as absolute cardiac arrest, as there is still a small residual circulation maintained by the left side of the heart as evidenced by a continual flow of blood from the coronary sinus and the presence of a weak pulse in the carotid artery[12] throughout the 12 minute tie-off period in a dog at 26 degrees C. This leads to the supposition that a human might tolerate satisfactorily six minutes of caval occlusion at normal body temperature. Templeton and Gibbon[13] demonstrated that dogs at normal temperature could tolerate nine minutes of caval occlusion. Out of 19 animals, seven died and three had gross neurological damage. This should be contrasted, perhaps, with our series of 27 animals with 12 minutes occlusion at 26 degrees C. with four deaths and one case of gross neurological damage. Probably eight minutes is a more satisfactory length of time for caval occlusion in a dog at normal body temperature. In that case, hypothermia at 26 degrees C. would safely allow a dog a 50 per cent increase in occlusion time. Applying the same rule to man would indicate nine minutes as being safe at 26 degrees C. At the present time there are reports in the literature of caval occlusion being used for intracardiac surgery in humans.[14,15] However, the time of occlusion was quite brief and would not be sufficient to allow definitive surgery on the valves or septa.

SUMMARY

1) By the use of hypothermia, metabolism and oxygen requirements of the body may be decreased. With such a method, the period of circulatory arrest can be increased to such an extent that direct intracardiac surgery for definitive repair of valves and septa may be possible.

2) We have presented our technic for an efficient and safe method of producing hypothermia in the experimental animal.

3) By the use of caval occlusion, a relatively bloodless heart can be obtained. Such a method has allowed us to perform cardiotomy on the right auricle and right ventricle for varying periods of time (12 to 30 minutes). This much time would obviously be sufficient for definitive surgery upon the valves and septa.

4) We have presented a preliminary report concerning the technic of hypothermia and cardiotomy. The procedure was performed on 32 dogs, with survival in 80 per cent of the animals

with caval occlusion for 12 minutes, and 40 per cent survival in those having caval occlusion for 30 minutes.

5) It is our feeling that such a method will be useful in the surgical management of various disorders of the circulatory system—in particular, defects of the auricular and ventricular septa.

RESUMEN

1) Con el uso de la hipotermia, el metabolismo asi como el requerimiento de oxigeno por los tejidos, se encuentra disminuido. Con el uso de este metodo, la circulación sanguinea puede ser interrumpida por un tiempo mayor, de modo tal que la definitiva corrección de defectos valvulares y septales, sea posible.

2) Hemos presentado nuestra tecnica de producción de una eficaz hipotermia en el animal de experimentación.

3) Ocluyendo las venas cavas, es posible obtener un corazón relativamente exangue. Este metodo nos ha permitido realizar cardiotomias, tanto en la auricula como en el ventriculo derechos por periodos variables de tiempo que ocilla entre 12 y 30 minutos, tiempo suficiente para actuar directamente sobre valvulas y septo.

4) Hemos presentado una comunicación preliminar concerniente a la tecnica de la hipotermia y de la cardiotomia. Este procedimiento ha sido efectuado en 32 perros. La sobrevida fue de 80 por ciento cuando las venas cavas fueron ocluidas por espacio de 12 minutos, habiendo sido de solo 40 por ciento cuando la oclusión se mantuvo 30 minutos.

5) Creemos que un metodo como el presentado sera de gran utilidad en la corrección de diversas afecciones del sistema circulatorio, y en particular en el tratamiento de cardiopatias congenitas.

RESUME

1) L'hypothermie reduit le métabolisme cellulaire et ainsi la demande d'oxygene. Par telle métode il devient possible de prolonger le temps de l'arrêt de la circulation aussi longtemps que l'on puisse procéder des opérations intracardiaques directes, soit pour lésions valvulaires ou pour lésions de la cloison intraauriculaire ou intraventriculaire.

2) Les auteurs présentent leur technique pour arriver sans danger a une hypothermie efficace.

3) En bloquant les veines caves, ils obtiennent des chambres cardiaques qui sont relativement vides et ils peuvent ainsi procéder la cardiotomie et opérer sous vue directe pendant 12 a 30 minutes, temps suffisamment long pour réparer definitivement valves ou cloisons.

4) Les auteurs présentent un rapport préliminé sur la technique de l'hypothermie. 32 chiens ont été traités de tels procédés. 80%

des animaux ayant eu un blocage dos veines caves pendant 12 minutes, 40% des animaux ayant eu un blocage pendant 30 minutes ont survécu.

5) Les auteurs croient que tels procédés seront utiles pour le traitement chirurgicale de certaines maladies cardiaques ou vasculaires, en particulier des lesions de la cloison interauriculaire ou interventriculaire.

ACKNOWLEDGEMENTS

We would like to thank Dr. J. DePalma, Head of the Department of Pharmacology, for his valuable advise and his extreme generosity in placing the facilities of his laboratory at our disposal. We would also like to express our debt to Mr. Frank Rajkowski, our technician, whose interest and loyalty made him work countless unpaid hours and made many useful contributions. Finally, we are indebted to our nurse, Miss Ruth Apler, who contributed greatly to the smooth running of the surgery.

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Cor Pulmonale (Pulmono-Cardiac Syndrome) A Case Report*

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Little information is available concerning the cardiovascular and respiratory adjustments in patients suffering from heart failure secondary to marked chest deformities. These cases represent extreme examples of pure "cor pulmonale" and the observations reported below are thought to be of interest in relation to similar studies on subjects suffering from a variety of obliterating pulmonary vascular diseases with secondary heart involvement.[1]

Only a few instances of this syndrome in young individuals have been studied by modern methods and the extreme changes observed are therefore thought to be of interest.

Case History

B.B., a 13 year old white girl, was well until the age of three years, when scoliosis with convexity to the right was first noted on a routine x-ray film of her chest. Following this observation the child was given physiotherapy and appropriate exercises, and wore back braces for many years.

She had no symptom referable to her cardiovascular system except a moderate decrease in exercise tolerance until 18 months prior to admission, when she developed cyanosis, anorexia, nausea, malaise, cough, tachycardia, and swelling of the face. On the basis of cyanosis and coexisting congenital anomalies of the skeletal system, she was thought to have a congenital malformation of the heart. She was hospitalized because of signs of congestive heart failure, and improved within three to four days on digitalis, oxygen, and bed rest. Following the first admission, the child was further hospitalized with similar signs and symptoms on five different occasions and each time responded well to the same therapy. Digitalis was discontinued after each episode. On October 30, 1950 she was transferred to this hospital for further studies prior to a possible surgical correction for congenital heart disease.

Physical examination at this time revealed an alert and cooperative young girl with a pulse rate of 100 beats/minute, respirations 24/minute, and blood pressure of 120/80 mm. Hg. in both arms and 122/84 mm. Hg.

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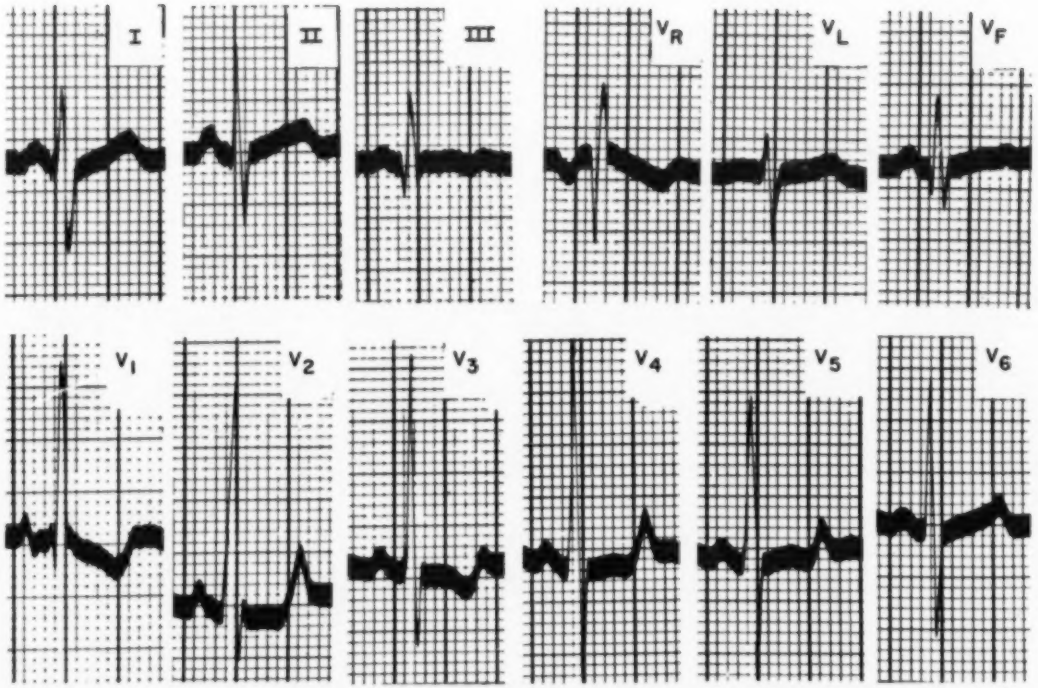

FIGURE 2: Electrocardiograms demonstrating a "vertically" placed heart with unusual cardiac rotation (prominent R in VR), and right ventricular hypertrophy (late intrinsicoid deflection with tall R waves) in V_1 to V_3.

in both legs. Height was 52½ inches and weight 73 pounds. She was small, fairly well nourished and did not appear acutely ill. A marked kyphoscoliosis was present with the convexity of the thoracic spine to the right (Figure 1). The right shoulder was higher than the left. The chest was severely asymmetrical, the right side demonstrating an increased AP diameter, and decreased lateral diameter compared to the left. The thoracic cage moved only minimally with respiration. Accessory muscles of respiration were not used. The diaphragm was low and moved poorly on both sides. The lungs were clear to percussion and auscultation. The heart was difficult to outline on percussion, but was not definitely enlarged. The heart sounds were normal. The remainder of the physical examination was within normal limits.

Routine laboratory data were not remarkable. The hemoglobin determination revealed 15 grams/100 cc. and the volume of packed red cells was 45 per cent.

X-ray film inspection of the chest was interpreted as showing severe scoliosis of the dorsal spine with convexity to the right and relatively normal sized heart (Figure 1). Cervical spine films demonstrated that "five normal cervical vertebrae are present, though the interspace between C4 and C5 is slightly less than normal and an attempted fusion may be present. The sixth cervical vertebra consists of two hemi-vertebrae which are unfused in the center. The seventh cervical vertebra is incorporated in a rather irregular dorsal spine and carries a rib." Dorsal and lumbar spine showed "a striking scoliosis with the curvature toward the left in the region of the dorsal spine which has been produced by extensive congenital anomalies involving most of the dorsal spine. The basis of the anomalies apparently is a failure of fusion of the right and left hemi-vertebrae over most of the dorsal segments which has resulted

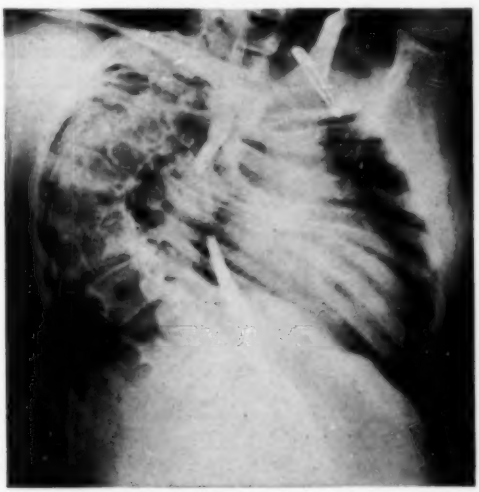

FIGURE 1: A.P. view of the chest demonstrating the extreme degree of skeletal deformity.

in a striking widening of the spinal canal. Excess hemi-vertebrae may be present in the upper dorsal spine. Innumerable rib deformities are present; several pairs of ribs, especially on the left, show a single common origin."*

The electrocardiogram (Figure 2) revealed a normal sinus rhythm with a rate of 100/minute; PR interval measured 0.14 seconds, QRS 0.08 seconds and QT 0.36 seconds (normal range: 0.29-0.36 seconds for this rate). Standard bipolar and unipolar limb leads suggested the heart to be vertically placed. A late R was present in VR. Very tall deflections with large R waves were noted in V1 to V4 and therefore no transitional zone could be detected. T waves were inverted in III, VR, and V1. The onset of the intrisicoid deflection measured 0.05 seconds in V1 (normal range 0.006 to 0.033 seconds). The record was interpreted as indicating marked right ventricular hypertrophy and, as such, appeared to be compatible with the diagnosis of congenital heart disease.

During the patient's hospital stay, the pulse varied from 60 to 120, respirations from 18 to 28, and temperature from 98.6 to 100 degrees F. She had no untoward symptoms during this period. On the 28th hospital day, a detailed study of her cardiorespiratory reserve was undertaken (Tables I and II).

Following this hospitalization she returned home and had no difficulty for three months. She then experienced a sudden onset of severe dyspnea, tachycardia, and cyanosis, as on previous occasions. She was admitted to another hospital and expired on the fourth day despite intensive treatment.

*X-ray films were interpreted by Dr. Henry P. Plenk, Associate Professor of Radiology, University of Utah College of Medicine.

TABLE I

Cardiorespiratory Studies on B.B. Compared with Similar Studies Performed in 12 Subjects with Cor Pulmonale and 10 Normal Volunteers[1]

Patient B.B.

	Rest	Exercise	Anesthesia	Cor Pulmonale (12)	Normal (10)
Pulmonary Ventilation L/min./M²	4.91	5.85	3.46	3.52	2.92
Oxygen Consumption cc./min./M²	199*	236	88	130	137
Oxygen Extraction cc./L ventilation/M²	40.5	40.5	25.5	38.5	48.1
Arterial Oxygen Content volumes per cent	—	—	15.15	13.50	17.90
Arterial-Mixed Venous oxygen difference volumes per cent	—	—	5.75	4.74	4.14
Cardiac Index	—	—	1.53	3.03	3.34
Pulmonary Artery Pressure mm. Hg.	—	—	(130/58) 82	(73/33) 46	(26/11) 16

* Not basal.

*Autopsy Findings**

The significant findings were confined to the chest and its contents. The dome of both the left and right hemi-diaphragms was at the sixth intercostal space. The diaphragm was about twice the normal thickness. Only a small amount of clear fluid was present in the pleural spaces. The rotation of the spine caused the thoracic vertebrae to lie within the right hemi-thorax. No adhesion was present. The lungs were small and compressed. The right lung weighed 290 grams, the left 230 grams (compared to an average weight of 200 grams each for a child this age). The surfaces were smooth and glistening. Both lungs were dark bluish-red and were non-crepitant throughout. On cut section, the tissue was dark to light mottled red. A foamy bloody fluid exuded slightly on pressure. The bronchi and pulmonary vessels were patent. Their lumina were not remarkable. The lower lobe of the left lung was considerably smaller than the upper lobe. The pericardium contained about 50 cc. of thin yellow fluid. No adhesions were present. The pericardial surfaces were smooth and glistening. The transverse diameter of the heart measured 10 centimeters, the vertical diameter 8.5 centimeters. The conus region of the right ventricle and the pulmonary artery were prominent.

The pulmonary artery was approximately one-third larger than the aorta. The diameter of the ascending aorta was 1.8 cm., and the diameter of the pulmonary artery was 2.6 cm. The heart weighed 240 grams (as compared to a normal weight of 124 grams). The myocardium was firm and light red-brown. The endocardial surfaces were smooth and glistening. No evidence of congenital malformation or abnormal intracardiac shunts was present. The tricuspid valve measured 9.0 cm. and the aortic valve 5.0 cm. All valves were smooth. The left ventricular wall measured 1.2 cm. in thickness. The conus of the right ventricle was 0.6 cm. thick. The coronary ostia and coronary arteries were patent.

*Autopsy performed by Dr. John H. Carlquist, Associate Clinical Professor of Pathology, University of Utah College of Medicine.

TABLE II

Vascular Resistance and External Work Performance in B.B. Compared with Similar Studies Performed in 12 Subjects with Cor Pulmonale and 10 Normal Volunteers[1]

Patient B.B.

	Anesthesia	Pulmonale (12)	Normal (10)
Total Peripheral Resistance (dynes/sec./cm.^{5})	4420	1488	1150
Total Pulmonary Resistance (dynes/sec./cm.^{5})	3900	813	189
Right Heart Work (KgM/min./M^2)	1.80	1.92	.90
Left Heart Work (KgM/min./M^2)	2.04	3.59	4.37
Ratio: {Left Heart Work / Right Heart Work}	1.13	1.88	5.46

Microscopic sections of the lungs showed passive congestion and atelectasis. Many alveoli contained red blood cells and many large monocytes containing blood pigment. The small arterioles showed slight but definite thickening of the walls. Histologic sections of the heart were not remarkable.

Further Observations

This girl represents a case of severe "cor pulmonale" usually referred to as "pulmono-cardiac syndrome" and due to congenital kyphoscoliosis.[2] All clinical findings pointed to cor pulmonale with little evidence in favor of a congenital defect.

Detailed studies of her cardiorespiratory function revealed reduced vital capacity (600 cc.) with normal resting pulmonary ventilation (Tables I and II). Somewhat surprisingly, oxygen extraction per liter ventilation was normal at rest and revealed no decrease on exercise. A fall in oxygen extraction is a sign of severe impairment of pulmonary flow and may be used as an important finding in subjects with intra-cardiac shunts.[3] It also occurs in many patients with acquired disease and cor pulmonale.[1] Mixed venous and arterial oxygen saturation were low. Multiple sampling of right heart blood during cardiac catheterization revealed no evidence of abnormal intra-cardiac arterio-venous shunts.

The pulmonary artery pressure obtained by a Statham strain gauge measured 130/58. In contrast, values of 26/11 mm. Hg. are found in normal subjects, and 73/33 mm. Hg. in adults suffering from heart disease secondary to acquired pulmonary pathology. With the exception of the values for pulmonary artery pressure, all findings are consistent with those found in adults who had been in congestive failure due to cor pulmonale secondary to chronic lung disease.[1]

She was not in heart failure at the time of these studies, and a zero diastolic pressure in the right ventricle indicated that right ventricular dilatation was absent. The right ventricular pressures were also excessively elevated (90/0 mm. Hg.). The slightly lower right ventricular systolic pressure was not recorded simultaneously with the pulmonary artery pressure. The electrocardiographic findings of right ventricular hypertrophy are more marked than is usual in subjects with pulmonary disease and correlated well with the excessive right ventricular pressures present. This observation and others of a similar nature in subjects with right ventricular hypertrophy corroborates the statement of Johnson et al.[4] concerning the correlation of electrocardiographic findings over the right ventricle to right ventricular and pulmonary artery pressures.

The cardiac output obtained by the direct Fick principle was low compared to that of normal controls. This may have been

secondary to the basal anesthesia (avertin) and heavy sedation (Nembutal, morphine sulfate, and scopolamine) under the influence of which the studies were obtained.

The total peripheral resistance was increased (Table II), primarily because of the lowered cardiac output. The total pulmonary resistance was markedly elevated to a point that approached the total systemic resistance. This increased vascular resistance was primarily due to the high pulmonary artery pressure. In consequence, the external work of the right heart, calculated by appropriate formulae,[5] was increased and the left heart work was decreased so that the ratio of left to right heart work was markedly reduced in comparison to the normal (Table II). The calculated external work performance of the right ventricle, usually one fifth of that of the left, almost equalled that of the left ventricle in this patient (left/right ratio 1.13) and was appreciably higher than that of other types of cor pulmonale studied in this laboratory (left/right ratio 1.88). The pulmonary artery pulse pressure was moderately increased.

The high pressures in the pulmonary circulation were thought to be an expression of an extreme degree of pulmonary vascular resistance secondary to vascular sclerosis, or spasm, fixed, poorly moving diaphragm, and a decrease in actual lung space. This, in turn, appeared to be the result of a fixed pulmonary bed which lacked the usual resilience and adaptability noted by Cournand,[6] and the "check valve" characteristics pointed to by McCann.[7] Kinking of the pulmonary artery, often stated to be a cause of right ventricular failure in the pulmono-cardiac syndrome,[8] was considered unlikely in this patient because the cardiac catheter could be placed with ease into the distal artery segment and recorded pressures were identical in distal and proximal segments of the pulmonary artery. No kinking of either pulmonary artery or aorta was found at autopsy.

The earlier contention[2] that severe impairment of the pulmonary bed may lead to right ventricular hypertrophy and heart failure is supported by these studies which seemed to demonstrate that, above all, the alterations in vascular pressures were primarily responsible for the syndrome of cor pulmonale in this patient.

SUMMARY

1) A case of pulmono-cardiac syndrome is presented. Detailed clinical and physiological studies were made and autopsy data are also recorded. The outstanding physiologic characteristics were the striking elevation of pulmonary vascular pressures resulting in work loads of the right heart approximately equalling that of the left.

2) The findings in this case are compared to findings in a group of adults with "chronic cor pulmonale secondary to chronic lung disease," which they closely resemble.

RESUMEN

1) Un caso de síndrome cardio-pulmonar se presenta. Estudios detallados clínicos y fisiológicos fueron hechos y se refieren los datos de la autopsia. Las características fisiológicas más notables fueron la súbita elevación de las presiones pulmo-vasculares, resultantes de cargas de trabajo del corazón derecho, igualando aproximadamente las del corazón izquierdo.

2) Lo encontrado en este caso es comparado con lo hallado en un grupo de adultos con "cor pulmonale secundario crónico en enfermedad crónica del pulmón" al que se asemejan mucho.

RESUME

1) Les auteurs rapportent un cas de syndrome cardio-pulmonaire. L'étude clinique et physiologique en a été poursuivie et les résultats de l'autopsie sont également mentionnés. Les caractéristiques physiologiques remarquables furent l'élévation frappante des pressions de la circulation pulmonaire, conséquence de l'activité du coeur droit, qui arrivait à être à peu près égale à celle du coeur gauche.

2) Ces constatations ont été comparées avec les résultats de l'examen d'un groupe d'adultes, atteints de coeur pulmonaire secondaire à une affection chronique du poumon. Il y a entre les deux ordres de faits des ressemblances très proches.

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The Coronary Circulation in Patients with Severe Emphysema, Cor Pulmonale, Cyanotic Congenital Heart Disease, and Severe Anemia*

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In a recent publication we have described a method of injection of the coronary arteries.[1] That work, a study of coronary artery patterns and their normal variations, utilized a modification of the Schlesinger injection technique. The injection mass used was a barium latex compound in which the particle size of the injection material had been standardized by screening viscosity determinations and ocular micrometer examination at 14 micra. The present study has to do with a particular phase of coronary artery circulation as demonstrated by the injection technique; namely the development of collateral or anastomotic circulation in patients with severe emphysema, cor pulmonale, cyanotic congenital heart disease, and severe anemia.

From the pathological physiology it can be seen that these four disease states have one thing in common and that is anoxia. In severe emphysema the oxygen saturation of the arterial blood may and does run, as low as 70 per cent. In our laboratory, studies of the arterial O_2 saturation in severe anemias, have been in the normal range, however, the O_2 carrying capacity may be reduced to below a third normal which results in a local O_2 want at the cell level, since only one-third of the normal amount of O_2 is being delivered into the cells. In cyanosis with polycythemia there is enough circulatory hemoglobin but once more, it is not carrying its full quota of O_2 so again there is a deficit in oxygen at the cell level.

Although it has been taught since the days of Conheim, that the coronary arteries were end arteries, it has gradually become accepted that an anastomotic circulation exists within the normal heart. That such an anastomotic circulation normally connects the capillaries and other finer vessels is indeed well established, and Gross, Spaltehoiz and Campbell, as a result of their studies,

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A portion of this work was done while the author was Director of the Cardiovascular Research Laboratory, City Hospital, Cleveland, Ohio. The author is indebted to A. F. Young, M.D., who aided in the routine injections during this period.

believed that with increasing age, an anastomotic circulation was also developed within pre-capillary vessels.[2,3] In 1940 Blumgart and his associates reported an investigative work which was not entirely in accord with this view.[5] They were unable to demonstrate any evidence of an anastomotic connection between the right and left coronary arteries in the hearts of patients in the seventh and eighth decades of life who had shown no evidence of cardiovascular disease and had only minimal coronary artery sclerosis. The injection material used for this study rarely penetrated the vessels of smaller caliber than 40 micra, however, and it is well known, that watery solutions injected into the right coronary arteries are regularly recovered in the branches of the left coronary artery and vice versa in normal hearts. It can be concluded, therefore, that the diameter of the connecting vessels is less than 40 micra. It seemed to us that the barium latex injection mass with a standardized particle size of 14 micra was ideally suited to the investigation of this problem, because while readily penetrating to vessels of pre-capillary diameter, the capillary beds themselves were not filled or visualized. It has been shown by Blumgart and his associates that anastomotic circulation invariably exists in relation to considerable narrowing or old com-

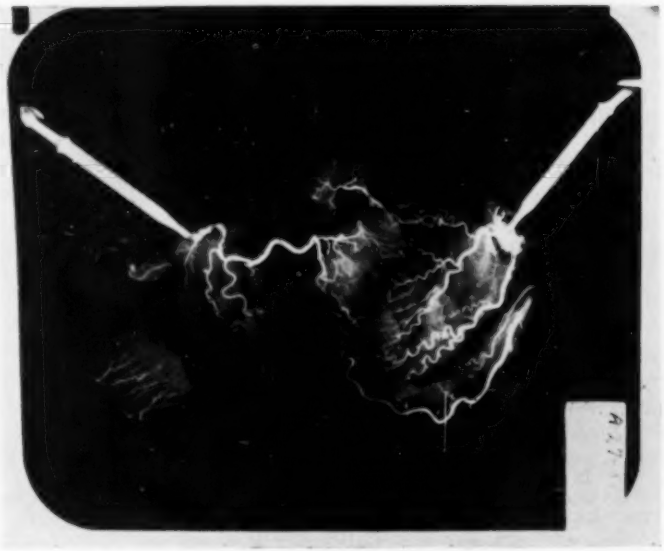

FIGURE 1: Shows a normal coronary injection with a right sided predominance.

plete occlusions of the coronary arteries and that anastomotic circulation is also found in the presence of rheumatic valvular disease or arterial hypertension with little or no coronary artery narrowing or occlusion. We have, therefore, largely confined the present investigation to a study of the coronary circulation in patients with cor pulmonale, cyanotic congenital heart disease, and severe anemia. In the review of material from our first 165 cases, we have found 13 cases with a very significant increase in the small ramifications of the coronary arteries, which were visualized by x-ray examination after injection of the barium latex mixture by the previously described technique. Of these 13 cases, six are of cor pulmonale, three are of chronic severe pulmonary emphysema, one is of aplastic anemia, two are of untreated pernicious anemia and one is of congenital heart disease with cyanosis and polycythemia. Figure 1 reveals the coronary circulation in a normal heart which has been prepared by the injection technique. Figure 2 shows the heart of a patient with cyanosis and polycythemia. A comparison of these two figures readily demonstrates a marked increase in the number of small coronary branches visualized in the right and left ventricles of the injected specimen, so much so in the right ventricle as to approach in

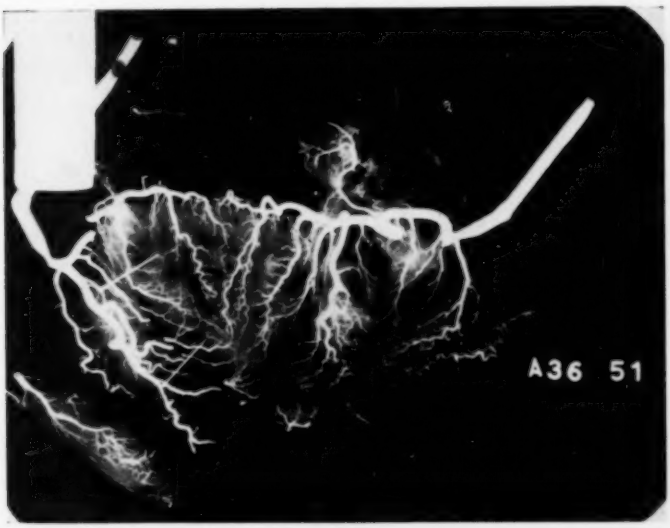

FIGURE 2: The coronary circulation in a heart from a case of congenital cyanotic heart disease, note marked increase in development of anastomotic vessels.

number the ramifications of the left ventricle. These findings were consistently shown in all of the 13 cases mentioned above. The myriad ramifications of the coronary tree are readily seen even in the reproductions.

The experimental studies to date do not afford an explanation of the various factors involved in the development of this anastomotic circulation. The only reference to collateral coronary circulation in anemia which we have found in that of Amadeo[6] who hypothecated on purely clinical grounds that anemia may effect a beneficial effect on the heart by compelling it to develop a special compensatory mechanism to offset the attendant myocardial anoxia. He further hypothecated that this mechanism might well be the reduced blood viscosity of anemia which could open up existing but nonfunctioning coronary artery connections. This theory would not explain the increase in number of anastomotic channels found in cases of cor pulmonale, many of which have polycythemia and increased blood viscosity. Patients with cor pulmonale do show anoxemia and a low oxygen saturation of arterial blood may be the initiating factor in the development of the collateral circulation. We submit, therefore, that it is the increased local cardiac need or perhaps myocardial anoxia which is the primary factor in the development of such circulation, regardless of whether that need is occasioned by increased work of a part of the myocardium, coronary artery insufficiency, or decrease in the amount of circulating oxygenized hemoglobin from any cause whatsoever.

SUMMARY

This paper deals with the coronary circulation in patients with severe emphysema, cor pulmonale, cyanotic congenital heart disease and severe anemia.

RESUMEN

Este trabajo se refiere a la circulación coronaria en los enfermos con enfisema severo, cor pulmonale, enfermedad congenita cianótica cardiaca y anemia severa.

RESUME

Cette communication a trait à la circulation coronarienne chez les malades atteints d'emphysème sévère, de coeur pulmonaire, de cyanose congénitale et d'anémie grave.

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Pectus Excavatum*

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Pectus excavatum is a congenital deformity having insidiously progressive physiological and psychological manifestations. The essential abnormality (Figure 1) of pectus excavatum or funnel chest is posterior angulation of the gladiolus. The manubrium is not appreciably displaced. The gladiolus slopes toward the vertebral bodies. The xipho-sternal junction may even be in contact with the vertebral body. The costal cartilages attaching to the gladiolus slope sharply inward to their chondro-sternal articulations. The etiology of this condition is not clear, but there is a substernal fascia which appears to fix the lower end of the sternum. The heart is displaced to the left in direct proportion to the degree of deformity. The defect often is progressive with growth. The antero-posterior diameter of the central tendon of the diaphragm and its sternal attachments apparently remains relatively constant as the thorax grows. Brodkin[1] in a study of the development of the diaphragm from four embryological divisions, has found that the anterior division is tendinous and rigid in pectus excavatum.

The physiological handicap is gradual. It is first manifested by decreased endurance and later by dyspnea, palpitation and occasionally cardiac arrythmia. Dorner[2] believes that the limitations are due to displacement and compression of the heart. He demonstrated by angiocardiography enlargement of the right atrium and ventricle with distortion of the tricuspid valve all of which disappeared when the deformity was corrected surgically. Electrocardiograms are not reported to be distinctive. They usually show right axis deviation and other abnormalities difficult to interpret.

The psychological damage of this deformity to a child or even to an adult may be severe. The embarrassment and withdrawal of some deformed people, especially children, are too obvious to require elaboration. For cosmetic reasons alone we would feel justified in surgical correction in individuals with distinct de-

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formity. Most, however, also have cardio-respiratory handicaps although some are not aware of the handicap, having never experienced normalcy.

Numerous techniques have been described for the correction of pectus excavatum. Ochsner and DeBakey[3] stimulated the development of the procedure by a review of the literature and a case report in 1939. Brown[4] advised simple elevation of the sternum and freeing of the substernal ligament in infants. In addition, he advised for children and adults that the deformed costal cartilages be removed, a wedge be removed from the upper end of the deformed section of the sternum and that the sternal deformity be overcorrected.

Lester,[5] Sweet,[6] Ravitch,[7] and Brodkin[1] have all reported on further experience. Temporary external traction to maintain the elevation of the sternum has been advocated with varying degrees of success. Brodkin used internal stabilization; he fixed a piece of cartilage to the lower end of the sternum and attached its ends to the costal margins. Dailey[8] and later Dorner[2] used an inverted rib as a strut beneath the sternum to maintain its elevation. It was this modification which appealed to us and leads us to report our experience.

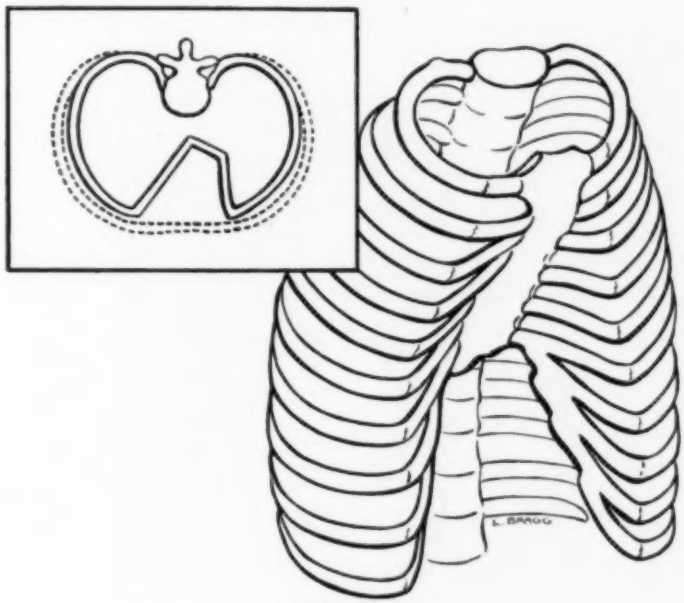

FIGURE 1

Technique (Figure 2)

The patient is anesthetized by general anesthesia using an endotracheal tube, and intravenous blood is given as in any major intrathoracic procedure. The incision is in the midline from just above the upper end of the deformity to half way from the xiphoid to the umbilicus. The skin flaps including the insertions of the pectoral muscles are dissected back to expose the thoracic cage back to a point just lateral to the deformed costal cartilages. The upper end of the rectus fascia is exposed and the xiphoid separated from the gladiolus. A wedge is made in the lateral end of the deformed portion of each costal cartilage so as to allow its elevation. A wedge is cut from the anterior cortex of the sternum across the manubrio-gladiolar junction and the sternum is then elevated. This is made possible by incising the attachments of the rectus muscles and dividing beneath the sternum its diaphragmatic and pericardial attachments. The elevation is maintained as follows: (1) Ends of the elevated costal cartilages are sutured to the side of the sternum after cutting off a small piece to allow an accurate fit; (2) The anterior cortex of the gladiolus is sutured to the opposing anterior cortex of the manubrium; and (3) The sternum is supported with one or two inverted ribs. The

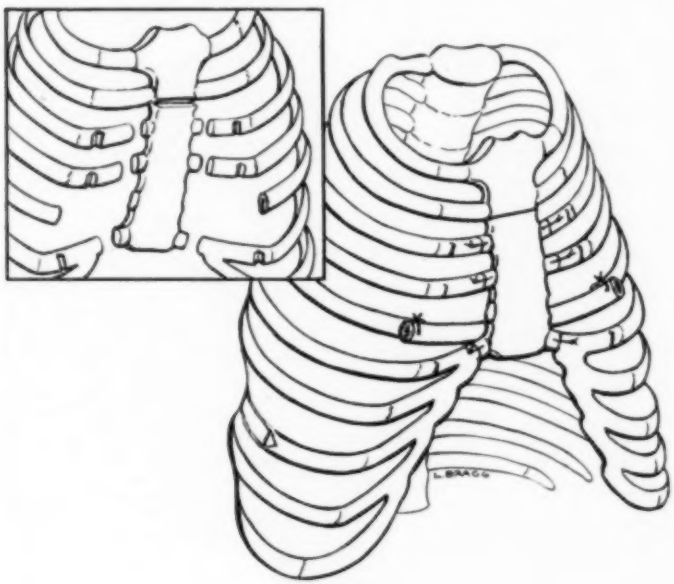

FIGURE 2

latter bridges from a rib on one side to that on the other and is fixed by sutures passed through drill holes in both the rib graft and the normal rib end. The skin flaps are closed over the corrected deformity. Should the pleura be opened accidentally, lung expansion is maintained by the anesthetist.

Case Reports

Case 1: D.B., a boy of three was seen because of a chest deformity. The mother noted the depression of the sternum at birth and felt that as the child grew it became more pronounced. She was not aware of dyspnea, palpitation, or limitation of the child's physical activity. Examination showed a healthy child in every way except for marked angulation of the sternum at the gladiolar-manubrial joint. The xiphoid was approximately 5 cm. below its normal level. The costal cartilages dipped into the side of the sternum giving a typical funnel chest deformity. The heart was displaced to the left (Figure 3). Operative repair was recommended, both for cosmetic reasons and because of the progressive nature of the deformity. Operation was carried out on September 28, 1950. The procedure was as described above. All suture material used was silk. A single inverted rib strut was used to support the sternum. It bridged from the end of the fifth rib on one side to that on the other. To allow room for the rib strut, the fifth costal cartilages were sacrificed completely. The rib was obtained through a separate incision by subperiosteal resection of a 9 cm. segment of the eighth rib on the right. The pleura was accidentally torn on both sides but lung expansion was readily maintained by the anesthetist. A catheter was left in the substernal space. Just prior to tying the last suture, positive pressure was applied by the

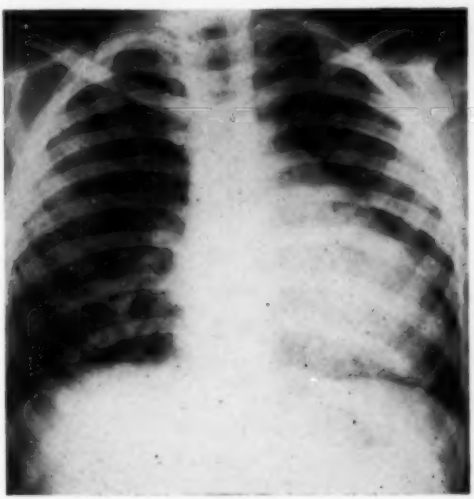

FIGURE 3

anesthetist expressing fluid through the tube which was then removed.

The postoperative course was uneventful. The child (Figure 4) was active within 48 hours and was discharged home on the seventh postoperative day. The wound healed per primam. The chest externally showed normal contour and function with no depression of the sternum. When last seen, April 10, 1951, the normal contour was perfectly maintained. X-ray film showed the position of the heart to be about as before operation, but there was normal elevation of the sternum. The autogenous bone graft appears to show some decalcification, but it is felt that at this time its support is no longer needed. The mother has noted a gratifying increase in the child's activity indicating an unrecognized limitation before operation.

Case 2: W.H., a 14 year old boy had noted funnel deformity of the chest since birth. With rapid growth in the past two years it seemed to progress. He could only participate in sports for a few minutes at a time because of dyspnea, palpitation, and even cyanosis. Examination showed a tall slender boy with a large depression of the sternum, which was angulated inward from the second costal cartilage. The right side of the sternum was more depressed than the left. Lateral chest x-ray showed the sternum depressed half way to the spine and but slight displacement of the heart to the left.

Operation was carried out under endotracheal ether oxygen on December 12, 1950. The procedure was essentially as in the previous case, except that two rib struts, obtained from the bone bank, were used be-

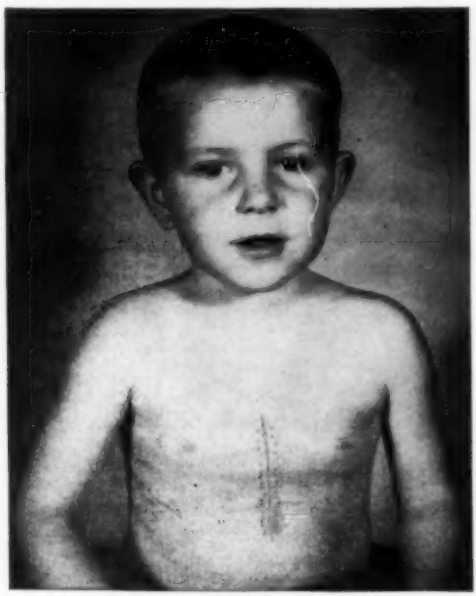

FIGURE 4

tween the fourth and seventh pair of ribs. The substernal space was drained for three days. The postoperative course was complicated by atelectasis which necessitated bronchoscopy and was prolonged by development of empyema, which required drainage. The operative area healed per primam. The end result was a normal chest contour. He was last seen April 28, 1951.

Discussion

The satisfactory end results reported justify operative correction of pectus excavatum. In general, the earlier the procedure is carried out, the simpler it can be. In infants, simple elevation of the sternum and division of the substernal attachments may be adequate. In older children and adults, results are uncertain unless some form of support is supplied. External traction requires passage of wire through the skin and must, therefore, be temporary. Even then infection is invited. The use of either autogenous or bone bank ribs as struts supplies support of indefinite duration. It is simple and satisfactory. It avoids the use of foreign material and leaves no tract for infection to enter. Early mobilization of the patient is possible.

SUMMARY

Pectus Excavatum (funnel chest) is a progressive deformity often with increasing cardio-respiratory handicap. The psychological handicap in children may be serious. The technique of operative repair is now developed. Support of the elevated sternum by a rib strut has proved satisfactory. Two such cases are described.

RESUMEN

El pectus excavatum es una deformidad progresiva que a menudo acarrea incapacidad cardio-respiratoria progresiva. La desventaja psicológica en los niños puede ser grave. La técnica de reparación operatoria ha progresado. El soporte del esternón elevado por medio de un segmento de costilla ha probado ser satisfactorio. Dos de esos casos son descritos.

RESUME

Le thorax creux est une déformation progressive qui s'accompagne souvent de troubles cardio-respiratoires croissants. Les conséquences psychologiques peuvent être sérieuses chez les enfants. La technique du traitement chirurgical est maintenant tout à fait au point. Le maintien du sternum par un greffon de côte s'est montré satisfaisant. Les auteurs rapportent deux cas de cet ordre.

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Discussion

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I began to study this condition before the war and have published several observations concerning this and two other related deformities. The three anterior chest wall deformities commonly referred to as pectus excavatum, pigeon breast, and Harrison's groove (each has many other names) have congenital etiology, namely an abnormally developed and an abnormally contracting diaphragm. This relationship is supported by the fact that they have several characteristics in common.

1) These deformities are present at birth with the first inspiration and are synchronous with the contraction of the diaphragm.

2) Each deformity is mobile during infancy and gradually becomes fixed at about the age of three, because of the lessening of the elasticity of the thoracic cage.

3) The extent of the deformity is probably dependent on the extent of the abnormality of the anterior portion of the diaphragm. Therefore, the deformity may be slight, moderate or severe and one side may be more affected than the other.

4) Injection of novocaine into the phrenic nerve of an infant with any of these deformities will reduce the inspiratory retraction on the same side, demonstrating the effect of the diaphragm.

5) Each deformity is the result of certain characteristic changes in the anterior ribs and sternum.

If one observes the breathing of a normal infant, the chest is round and immobile. The normal diaphragm, whose circumferential radial musculature arises along the thoracic outlet, and its insertion is in the trefoil membranous portion, contracts without any retraction of the anterior chest wall. If, however, the anterior segment of the diaphragm, derived from the septum transversum is lacking in muscle fibers or is tendinous, it will

act as a tendon or insertion and will pull on its anterior attachment namely the gladiolar xiphoid junction. It will continue this inspiratory pull until the anterior chest wall is brought into its fixed position, when the infant is about the age of three, resulting in a depression of the chondrosternal area. The mechanism of the production of the other two deformities is similar but are due to a specific variation in the relationship of the muscular and membranous portions of the anterior segment of the diaphragm. This, I have described in my publications. Therefore, the evidence is sufficient to state that these three deformities are the result of the abnormal contractions of an abnormally developed diaphragm pulling on its anterior attachment. I have, therefore, suggested the terms congenital chondrosternal depression, congenital chondrosternal prominence and congenital chondrocostal grooves for these three deformities.

If one keeps in mind the mechanism of the mobile deformity in infants with congenital chondrosternal depression and development of the fixed alteration sin the older group, the rationale of the treatment becomes clear. In infants there has been no alteration of the ribs and sternum and all that is necessary is separation of the anterior diaphragmatic attachment from its sternal attachment at the gladiolar-xiphoid junction. This comparatively minor operation I have termed phrenosternolysis. This will lessen the retraction at once. I have never noted any abnormality of the retrosternal ligament first emphasized by Brown.

In older children and adults, the ribs and sternum are angulated and fixed and require excision and shortening of the angulations of the ribs and elevation of the sternum. This operation I have termed chondrosternoplasty and in principle is the same operation described by the authors and Brown with certain modifications. An inverted Y incision is employed because it greatly increases the exposure and permits the removal of a portion of the lowermost anterior certilage to be used as a scaffold for the elevated sternum. It is placed at the lower edge of the sternum so as not to impose on the heart. Both of these procedures were described in detail in the March 1951 issue of *Diseases of the Chest*.

Many questions to this problem are still to be answered. One, for example: How early should one operate in the case of an infant? This operation should be done as early as possible. Recently, however, I have seen two new-born infants with well established chondrosternal depressions for whom surgery was advocated at once. Both gradually improved so that at the end of six weeks the chests appeared normal. The only apparent answer to me is that the anterior portion of the diaphragm was relatively deficient in muscular fibers but they continued to develop after

birth. It now appears that one should wait for several months before advocating surgery. The youngest patient in my series was five months of age. The less mobile the deformity is in the infant, the less improvement can one expect with a phrenosternolysis.

The indications for surgery in infants is to prevent the subsequent fixed deformity of the ribs and sternum. In the older group, I have advocated chondrosternoplasty in moderate to severe cases when first, psychoneurotic fixation is present and has not responded to psychotherapy; and second, when cardiorespiratory symptoms are present.

I have operated a total of 12 patients with most satisfactory results. This represents a small number of those that have consulted me for this condition. The largest group have been the adolescent male to whom a big round chest has been a sign of strength and the flat and depressed chest a sign of weakness. This operation is too involved to warrant just a cosmetic repair. However, if the mental state and attitude can be restored to normal, and the physical stamina can be improved in these patients, then this operation is justified.

Clubbing of the Digits as a Primary Disease*

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Introduction

Clubbing of the digits has been the subject of careful study for many years. It has been shown to occur in association with a large number of unrelated diseases but most frequently with intrathoracic disease. It has also been described as occurring in otherwise healthy individuals and to be present as an hereditary trait. To emphasize the fact that clubbing of the digits does not of itself indicate the presence of visceral disease, the subject is reviewed and additional cases of primary clubbing are presented.

Review of the Literature

Witherspoon[15] summarized the reported instances of hereditary clubbing appearing in the literature prior to 1936. There were 33 cases of clubbing occurring in more than one generation in nine families. In addition there were two families in each of which two siblings, in one family twins, demonstrated clubbing. Witherspoon then added a description of a Negro family studied personally in which six members representing two generations had symetrical clubbing of all fingers and toes. Horsfall[7] presented observations on clubbing in 20 members of three families representing four generations in one family and three generations in two families. In two of 10 members with clubbing in one family only the thumbs and great toes were involved. The remaining members of this family with clubbing and those with clubbing in the other two families showed a symetrical involvement of all fingers. There was involvement of the toes as well in 10 cases. Seaton[13] described four members in three generations of one family with symetrical clubbing of all fingers and toes. Davis[5] presented one family in which seven members in five generations demonstrated bilaterally symetrical clubbing of the first three fingers and toes. All the members with clubbing and many others in the family without clubbing had webbing of the second and third toes. A second family was studied by Davis in which four members in two generations had clubbing of the little fingers only, the degree of clubbing being unequal bilaterally. Jackson[8] added descriptions of two families, each with two members in two generations demonstrating clubbed fingers.

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Thus clubbing has been described as occurring in more than one generation in 78 persons in 18 families.

Although additional cases of hereditary clubbing have been described, they have been associated with other developmental defects and therefore not considered to be examples of simple hereditary clubbing.

Neurath[12] described clubbing of the thumbs and great toes occurring in more than one generation in four families. As the defect was secondary to an alteration of the terminal phalanges, it would more properly be termed brachyphalangia. In the family described by Bernard[3] in addition to clubbing of the fingers, there was an hereditary absence of the thumb nails and large spade hands bilaterally. The digital lesions in the families studied by Davis as described above may also have been secondary to other hereditary defects and not simple clubbing.

Cases of clubbing have been described in whom no primary disease could be demonstrated.[1,8,9,10,13,14] These may be examples of hereditary clubbing, the patient or the examiner not being aware of the lesion in other members of the family. Also these may be cases of clubbing secondary to visceral disease not readily demonstrable. Such a situation existed in the patient described by Montuschi[11] where clubbing had been present since childhood. Only by thorough study including bronchograms was cystic disease of the lung demonstrated. Berg[2] presented a series of cases in

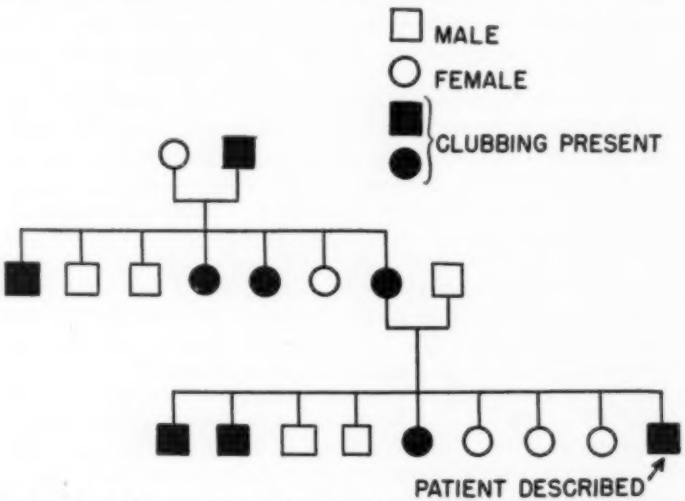

FIGURE 1: The occurrence of clubbing of the digits is shown diagramatically in three generations of the family in Case 1.

which clubbing secondary to intrathoracic neoplasm preceded by many months any evidence of the primary disease. Finally, there remain individuals in whom clubbing has been present for long periods of time and in whom no primary disease can be discovered despite thorough examination. These cases must be considered as examples of idiopathic clubbing.

Report of Cases

Case 1: W.E.W., a 28 year old, white male, was admitted to the hospital in August 1948, with complaints of chills and fever of one week's duration. On examination clinical and electrocardiographic evidence of pericarditis was present. There was clubbing of all fingers and toes which had been present as long as he could recall. Clubbing of the digits was present in the maternal grandfather, the mother, two maternal aunts and one maternal uncle, in two brothers and one sister (Figure 1). He became asymptomatic after two weeks' hospitalization and returned home after seven weeks' hospitalization. Examination 10 months later revealed him to be asymptomatic and working. The severity of the clubbing did not vary during the course of the pericardial disease.

Case 2: C.T., a 57 year old Negro male, was hospitalized in April 1949, complaining of arthritis and cough. Pain, stiffness, and limitation of motion had been present in the ankles, knees, hands, elbows, neck and back for 30 years. The severity of these symptoms had progressed since onset and had forced him to stop work eight years prior to admission. Chronic cough productive of mucous had been present during the same period of 30 years. He had noted large curved nails of the hands and feet since childhood, the degree of enlargement increasing with age. The only offspring, a 34 year old male had enlarged finger tips and nails similar to those of his father. Examination revealed moderate hypertensive cardiovascular disease, minimal pulmonary emphysema, and pain and

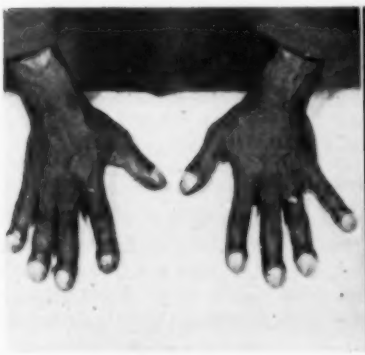

FIGURE 2

FIGURE 3

Figure 2: Photograph of the hands in Case 2, demonstrating the marked degree of clubbing. — *Figure 3:* A roentgenogram of the right knee in Case 2, showing the periosteal changes.

limitation of motion of the neck, back, knees and elbows. There was symetrical clubbing of all digits presenting a "parrott beak" appearance (Figure 2). X-ray film examination of the skeletal system demonstrated considerable broadening of the ungual phalanges bilaterally, extensive periosteal proliferation in both femurs, tibias and in the phalanges bilaterally (Figure 3). There were definite periosteal changes in the lumbar spine, pubic rami, both acromial processes and along the inferior margin of the left scapula. The only abnormal laboratory findings were elevated blood sedimentation rate and moderate normochromic anemia. Bronchoscopy revealed no abnormality, there being no inflammation, edema, or excessive secretions. Bronchograms demonstrated no evidence of bronchiectasis. There was irregularity of the outline of some of the bronchi thought to be due to bronchial secretions. The patient was discharged after four months' hospitalization.

Case 3: H.J., a 57 year old, white male was hospitalized in July 1948 because of recurrent joint pain. For 11 years prior to admission he had experienced recurrent episodes of swelling tenderness and increased heat in the fingers, wrists, elbows, ankles and knees. These attacks usually involved one joint at a time, occurred every two to three weeks, had a three day duration and resolved leaving no residual pain or stiffness. Examination revealed tenderness on pressure over the left knee and elbow and symetrical clubbing of all digits. He had been aware of the abnormality of the nails for more than 30 years. While under observation an episode of swelling, tenderness and increased heat in the right ankle occurred. X-ray film examination revealed no significant abnormality of the heart, lungs or skeletal system. All other studies were negative. No other members of the family were known to have clubbing.

Case 4: W.W., a 57 year old Negro male, was hospitalized November 1949 for treatment of an acute myocardial infarction. Examination revealed evidence of hypertensive cardiovascular and coronary artery disease. In addition there was symetrical clubbing of all fingers and toes. He stated that he had been aware of excessively large and curved nails since the age of 20 and felt that this abnormality may have been present for some years prior to that time. X-ray film examination of the chest revealed minimal cardiac enlargement and increased broncho-vascular markings in the lung fields. There was no x-ray evidence of periosteal changes in the long bones. The sedimentation rate was elevated and the hemoglobin depressed to a level of 10 grams. No other member of the family was known to be affected in a similar manner.

Discussion

An excellent example of hereditary clubbing of the digits is presented by the first case. The presence of the trait in members of successive generations of a family in a 1:1 ratio with no partiality to sex indicates the mode of transmission is by simple Mendelian dominance. This is in accord with the findings of other observers.[10,13] The second case does not present as precise a picture of hereditary clubbing. Although the abnormality was present since childhood, was present in the patient's son, and examination revealed only chronic bronchitis as a primary disease; a greater

number of cases in more generations would be desirable to firmly establish the diagnosis of hereditary clubbing. Nonetheless the patient presents a striking example of severe incapacitating hypertrophic osteoarthropathy in the absence of severe visceral disease. Cases similar to this have been described by Campbell[4] and Freund[6] using the term idiopathic familial generalized osteophytosis. In the third case it might be postulated that the joint disease was the primary factor, the clubbing occurring secondarily. However, since the clubbing preceded the joint pain by many years it seems more likely that it was the primary disease. Case four presents a picture that must be termed idiopathic clubbing as no organic disease could be demonstrated that might produce clubbing beginning at an early age.

The presence of clubbing in the cases reviewed and presented increases the complexity of the study of causative factors responsible for the development of this lesion. Although many theories have been advanced, none can satisfactorily explain the origin of clubbing in its many unrelated occurrences.

SUMMARY

1) Two cases of hereditary clubbing and two cases of idiopathic clubbing are described. The literature concerning this subject is reviewed.

2) Clubbing of the digits may be present as a primary disease and does not in itself indicate the presence of a visceral lesion.

RESUMEN

1) Dos casos de dedos hipocráticos hereditarios y dos casos de la misma deformación idiopáticos son descritos. Es revisada la literatura concerniente a este asunto.

2) Los dedos hipocráticos pueden presentarse como una enfermedad primaria y no indican por los mismos la presencia de una lesión de las vísceras.

RESUME

1) L'auteur donne la description de deux observations d'hippocratisme digital héréditaire et de deux observations d'hippocratisme digital idiopathique. Il passe en revue la littérature concernant ces sujets.

2) L'hippocratisme digital peut exister comme affection primitive et ne suffit pes à lui seul pour affirmer l'existence d'une lésion viscérale.

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The Influence of Cortisone on Tuberculin Shock in the Guinea Pig*

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There have been several reports indicating that cortisone suppresses or "blocks" the tuberculin skin reaction in man and experimental animals.[1-3] Also it has been shown that ACTH or cortisone inhibits the development of the Arthus phenomenon due to a suppression of antibody formation.[4] Recently it has been demonstrated that ACTH or cortisone did not prevent histamine effects on sensitized guinea pigs nor did these compounds decrease the mortality from anaphylactic shock in sensitized guinea pigs.[5,6] This differs from a report that cortisone prevented fatal anaphylactic shock in mice sensitized with horse serum.[7] Reinmuth and Smith[8] have demonstrated that ACTH administered to rabbits sensitized to M. tuberculosis and then injected intratracheally with Old Tuberculin had less extensive reactions than untreated controls. When ACTH was withdrawn, a fresh pneumonic consolidation occurred which was less severe than the reactions seen in the controls.

It was thought to be of interest to learn whether or not cortisone modified in any way the classical type of tuberculin shock in tuberculous animals.

Materials and Methods: Twenty-four male albino guinea pigs with an average weight of 350 g. were injected intradermally with 0.1 ml. 10 per cent Old Tuberculin and were found to be tuberculin negative. These animals were then inoculated subcutaneously in the groin with 0.1 mg. virulent human tubercle bacilli (H37 Rv) from a young liquid culture (Proskauer and Beck medium).

Twenty-five days after infection these guinea pigs were again tuberculin-tested in the manner described above. All animals were found to react to intradermal injections of Old Tuberculin. On the 27th day after infection, the animals were divided into two groups. Twelve received a daily intramuscular injection of 10 mg.

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cortisone acetate (Merck). Another 12 guinea pigs were injected intramuscularly daily with 0.4 ml. sterile physiological saline. These daily injections of cortisone acetate and saline were continued for five days.

On the fifth day of therapy (32nd day of infection) both groups of animals were injected intraperitoneally with 1.0 ml. concentrated Old Tuberculin. All survivors were autopsied 36 hours later.

A second experiment, employing 16 guinea pigs, was carried out in a similar manner to determine whether or not cortisone merely delayed the occurrence of the tuberculin shock. Instead of sacrificing the animals 36 hours after the intraperitoneal injection of concentrated Old Tuberculin, they were observed for 96 hours after the cortisone was discontinued.

Results: The results of the first experiment are summarized in Table I. All animals exhibited clinical evidence of anaphylaxis. The group that received the daily injections of saline demonstrated a more severe reaction than did the group treated for five days with cortisone acetate. Thirty-six hours after the intraperitoneal injections of concentrated Old Tuberculin, 11 of the 12 guinea pigs of the saline-injected group were dead, whereas only four of the 12 animals in the cortisone-acetate-treated group had died in the same period of time. Autopsy of the animals that died from

TABLE I

Effect of Cortisone on Tuberculin Shock in Guinea Pigs.
(36 hours after intraperitoneal injection of O.T.)

GROUP	Number Animals	Number Survivors	Per cent Survivors
H37 Rv Saline (0.4 ml. daily, 5x)	12	1	8.3
H37 Rv Cortisone Acetate (10 mg. daily, 5x)	12	8	66.6

TABLE II

Effect of Cortisone on Tuberculin Shock in Guinea Pigs.
(Observed for 96 hours after intraperitoneal injection of O.T.)

GROUP	Number Animals	NUMBER SURVIVORS				
		8 hrs.	24 hrs.	48 hrs.	72 hrs.	96 hrs.
H37 Rv Saline (0.4 ml. daily, 5x)	8	3	0	0	0	0
H37 Rv Cortisone Acetate 10 mg. daily, 5x)	8	7	4	3	3	3

shock in each group during the 36-hour period revealed active progressive tuberculosis, involving lymph nodes, lung, spleen, and liver. There was marked edema about the face, eyes, and feet. Their peritoneal and thoracic cavities contained a large amount of free fluid, usually quite bloody. The spleens and livers were hemorrhagic and in several cases ruptured. The cutaneous tissue at the site of the intraperitoneal Old Tuberculin injection was hemorrhagic and edematous.

The animals surviving for 36 hours in both groups recovered from the shock and were autopsied. The degree of tuberculosis was comparable to that found in animals which had died of tuberculin shock.

The results of the second experiment are summarized in Table II, where it can be seen again that cortisone afforded some protection against tuberculin shock. There was no significant delay in the development of shock since all of the deaths occurred within 48 hours.

Discussion: Cortisone seems to protect tuberculous guinea pigs from tuberculin type anaphylaxis. Whether the mechanism of action is mediated directly through some interference with antigen-antibody reaction, or whether the suppression of capillary dilatation and acute inflammatory reaction which has been noted with cortisone administration plays the major role, is not clearly understood at this time.

Autopsy studies of the animals which were sacrificed and those which died indicate that protection probably results from inhibition of capillary dilatation and hemorrhagic reaction.

SUMMARY

Cortisone acetate affords partial protection from the classical type of tuberculin shock in tuberculous guinea pigs.

RESUMEN

El acetato de cortisona proporciona un protección parcial contra la forma clásica del choque tuberculínico en los cuyes tuberculosos.

RESUME

La cortisone donne une protection partielle contre le choc classique que réalise la tuberculine chez le cobaye tuberculisé.

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Primary Tuberculosis Acquired in Adulthood*

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When primary tuberculous lesions were found so frequently in the lungs and hilum lymph nodes, it was assumed that the bacilli had entered through the respiratory tract. When mesenteric lymph nodes were involved it was thought that the invasion had occurred through the digestive tract. Inasmuch as many more lesions were found in the chest than in the abdomen, it was believed that the digestive tract was a far less common portal of entry than the respiratory tract. It is now known that regardless of where or how tubercle bacilli gain admission to the body, they may soon be deposited in various organs, even those remotely located from the site of entrance.

Chauveau (1868) was the first to demonstrate the transmissibility of tuberculosis by the digestive tract to various other organs, including the lungs, without leaving any trace of lesions in the intestine. Dobroklowski (1890) emphasized the ease with which the tuberculous virus could pass through the normal epithelium of the intestine without producing local lesions. Desoubry et al. (1895) showed that many kinds of bacteria pass through the intestinal mucosa during the digestion of fatty substances and for several hours are found in the chyle and the blood. Calmette, Ravenel and many others later demonstrated that when tubercle bacilli were introduced into the digestive tracts of animals they passed through the normal epithelial lining and appeared in chyle and blood within a few hours and later, in the lungs.

Krause injected tubercle bacilli subcutaneously in the inguinal region of animals and found them in the lungs, tracheobronchial lymph nodes and spleen in three or four days. Lemon and Montgomery placed tubercle bacilli directly into the pleural spaces of rabbits and found that some were soon deposited in remote organs. Vorwald introduced tubercle bacilli directly into the blood streams of animals and found them focalized in the lungs within an hour.

Initial Invasion of Tubercle Bacilli

Wherever tubercle bacilli enter the body by any route, including the respiratory tract, the digestive tract, the eyes, skin abrasions,

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or when they are deposited subcutaneously by a syringe into the layers of the skin by needle puncture or injected directly into the blood stream, they are promptly phagocytosed by neutrophils, which enter the lymph and blood streams. These neutrophils become toxic and lose their ability to change shape. Therefore, when they reach fine capillaries they are unable to pass through. Wherever they lodge in this manner the tubercle bacillus content is *focalized*. It is unlikely that all tubercle bacilli of the first invasion will be phagocytosed by a single neutrophil or that the many neutrophils which ingest them will be focalized in one place. Thus focalization may be in various places such as the brain, kidneys, spleen, liver, bones, joints and epididymis. Focalization is most likely to occur in organs richly supplied with fine capillaries, particularly the lungs. Therefore invasions of tubercle bacilli at any location in the body result in *bacteremia* before focalizations occur.

Wherever foci of tubercle bacilli appear, they are met by a *nonspecific response* of the body's defense mechanism which does not differ at first from foci of inanimate particulate material such as silicon dioxide. Usually the regional lymph nodes are soon involved, and these plus the primary lesions constitute primary tuberculosis complexes. Lesions of such complexes are generally benign and in most instances their presence is not detectable until the tissues of the body become so *allergic to tuberculoprotein* that they react characteristically to the tuberculin test. This degree of allergy is usually attained in people within three to seven weeks after the initial invasion of tubercle bacilli occurs. Therefore, the characteristic tuberculin reaction indicates the presence of primary tuberculosis complexes.

Tuberculin Reaction First Evidence of Presence of Primary Tuberculosis

When sensitivity of tissues can first be detected by the characteristic tuberculin reaction there is ordinarily no other manifestation of tuberculosis. In a small percentage of such cases, however, erythema nodosum may develop at this time and the erythrocyte sedimentation rate may be accelerated. The body temperature may be elevated to 100 or 101 degrees F. These findings usually do not persist longer than a few weeks to a few months, after which there is no evidence of tuberculosis except the tuberculin reaction.

X-ray inspection of the chest is of little avail in seeking locations of lesions of primary complexes because: 1) They are too small or are of such consistency that they do not cast visible shadows. 2) They may be in 25 per cent of the lungs obscured

from view by the shadows of other structures such as the diaphragm and heart. 3) Some are extrathoracically located.

In a few cases (rarely more than 5 to 8 per cent) there may be evidence of enlargement of hilum structures or shadow-casting pulmonary lesions, which Eliasberg and Neuland designated epituberculosis (1920-21). It is impossible to determine from the shadows whether the increased size of the hilum structures is due to tuberculosis. In fact, there may be definite disease in hilum lymph nodes without its presence being detected by x-ray film inspection, since these nodes must be large enough to encroach upon the pulmonary parenchyma before they are visualized with certainty.

The shadow-casting parenchymal lesions when caused by tuberculosis may be due to allergic reactions around one or more foci of tubercle bacilli or to atelectasis resulting from occlusion of bronchial ramifications from pressure of enlarged lymph nodes or exudate from the pulmonary lesion or ulcerative lesions in bronchial mucosa which obstructs their lumina.

When pulmonary lesions due to tuberculous foci and collateral inflammation are visualized they usually persist for some time—a year or so—after which they slowly resolve. When due to atelectasis only, the shadow appears no different than when caused by nontuberculous obstructions.

Primary tuberculous lesions are benign, because immediately after focalization occurs the bacilli are surrounded by walls of white blood cells and other defense elements. They develop in the same manner as silicotic nodules, that is, by nonspecific reaction of the tissues. When the silicotic nodule is well surrounded by fibrous tissue it has no further potentialities. When the tubercle is so encased, living organisms may remain within it over long periods of time, during which circumstances may develop that will permit them to produce clinical tuberculosis.

Within primary lesions may be found small areas of debris and necrotic tissue. In an occasional case this may be discharged into a bronchial ramification, leaving a small cavity. Even pulmonary hemorrhage may occur in such cases. Although primary pulmonary tuberculous foci may become sterile, postmortem examinations and excisions by recent surgical technic have revealed that they frequently contain an abundance of tubercle bacilli in necrotic centers and, hence, serve as a potential danger to future health.

In addition to fibrous tissue that is laid down in and around primary lesions there are often calcific deposits and sometimes pure bone formation.

Lesions that develop in the lymph node component of the pri-

mary complex frequently become necrotic and may contain tubercle bacilli over long periods of time.

Allergy Established

While primary tuberculosis complexes are developing, the tissues of the body become allergic to tuberculoprotein. This phenomenon is an asset to the physician in diagnosing the presence of primary tuberculosis by the tuberculin test, but it is a serious liability to the individual because tuberculoprotein, while innocuous to unsensitized tissues, is a deadly poison to those which are allergic—so poisonous in fact, that when it is injected into the skin or is eliminated from colonies of tubercle bacilli in the body, it kills cells and tissues with which it comes in contact, thus resulting in small and large areas of necrosis.

Benign Disease With Serious Future Potentialities

Although primary tuberculosis per se is a benign disease, it creates serious subsequent potentialities, as follows: 1) Lesions of primary tuberculosis complexes frequently harbor living virulent tubercle bacilli over long periods which at any time may result in acute or chronic reinfection forms of tuberculosis. 2) Allergy which results from primary tuberculosis is prerequisite for development of both acute and chronic reinfection forms of disease. The allergic body is prepared for such disease from both endogenous and exogenous reinfections with tubercle bacilli.

Long ago we adopted the concept that tuberculosis begins in animal and human bodies at the time tubercle bacilli are focalized by neutrophils and remains as long as living organisms are present. We have seen no reason to designate the condition tuberculosis only after gross lesions are present which can be detected by x-ray film inspection or when clinical manifestations exist. Moreover, we have not recognized a dividing line between infection and disease, since every person or animal infected so as to react to tuberculin possesses tuberculous lesions. The only difference between lesions developing at points of first focalizations of tubercle bacilli and those causing death from meningitis, miliary disease, extensive chronic lesions, etc., is one of degree. The individual developing primary lesions from first invasions has tuberculosis just as surely as the one dying from the disease. There is as yet no criterion by which the physician can determine which persons who acquire primary tuberculosis will become incapacitated. Suffice it to say that in all who become ill, the disease begins with the first focalization of tubercle bacilli and the intervals between this event and incapacity vary from months to decades.

The reaction of sensitized tissues to an invasion of tubercle

bacilli, whether they are from endogenous or exogenous sources, is specific and much more intense than that to an invasion of tissues that have not been sensitized. Therefore we have long regarded any lesion which has its beginning in sensitized tissues as the reinfection or clinical type.

Diagnosis

The diagnosis of primary tuberculosis is established by the tuberculin reaction. Symptoms when present do not differ from those caused by other diseases. Unless the primary lesions or component lymph node lesions are near the surface of the body, the conventional physical examination is of no avail. A small percentage of cases with shadow-casting lesions may be revealed by x-ray film inspection. After primary complexes have existed for some time (usually one year or more) evidence of calcium deposits may be seen in the lung parenchyma, hilum region, or both, in a small percentage of cases. No x-ray shadow is pathognomonic, since other diseases cast identical shadows. This includes calcific deposits.

Usually there is no cough or sputum caused by primary tuberculosis. However, tubercle bacilli may be recovered from gastric or bronchial washings in a small percentage of cases, particularly when shadow-casting lesions appear in the lungs. In this way bacilli are sometimes found when x-ray films reveal no evidence of disease.

Smears from accessible lesions, like those of the skin, mouth or thorat, may reveal acid-fast bacilli. Biopsy of involved superficial lymph nodes or lesions removed by excisional surgery may reveal microscopic evidence of tuberculous lesions as well as tubercle bacilli.

Treatment

Since the defense mechanism promptly corrals tubercle bacilli of the first invasion and controls the foci, usually no active treatment is indicated. The exceptions are:

1) When symptoms are present, strict bed rest is indicated only until they have subsided and the erythrocyte sedimentation rate has returned to normal.

2) If atelectasis is demonstrable, bronchial obstruction should be overcome as promptly as possible, otherwise bronchiectasis may later appear in the atelectatic areas. When bronchoscopy reveals bronchial obstruction due to extrinsic pressure, presumably from involved lymph nodes, or is due to exudate from the pulmonary lesions, or ulcerative lesions are seen in the bronchial mucosa,

streptomycin and para-aminosalicylic acid provide the most prompt relief.

3) Contagious disease technic usually is not necessary except during coexisting attacks of acute bronchitis, when those with tubercle bacilli recovered from gastric or bronchial washings may expectorate them.

4) Exogenous reinfections are dangerous and may result directly in chronic clinical forms of tuberculosis since the tissues are already sensitized when they occur.

5) Periodic examinations are important for every person who has primary tuberculosis because each one is a potential case of clinical disease. Among children, extrathoracic clinical lesions are not uncommon, particularly in bones and joints. Rarely do chronic pulmonary lesions appear before adolescence approaches. Among those who are 12 years or older, periodic examinations should include x-ray film inspection of the chest.

6) For primary pulmonary residuals some physicians now believe that excisional surgery is indicated, since postmortem examinations have long revealed that some such lesions contain necrotic areas bearing tubercle bacilli. While it may be advisable to remove such lesions, one must not forget that regional lymph nodes are also involved and that there is great likelihood that primary complexes and nodular lesions exist elsewhere in the body. Therefore the disease is not cured by surgery and regular periodic examinations should be continued.

7) To date, drug therapy is not indicated except in special situations such as the presence of ulcerative lesions in the bronchial mucosa, atelectasis, etc. If long term administration of streptomycin and para-aminosalicylic acid as is now being studied or another drug should be found which destroys tubercle bacilli in human tissues, the best time for administration will be as promptly as possible after primary tuberculosis is detectable, namely, when the individual converts from a nonreactor to a reactor to tuberculin. At that time the lesions are usually small and vascular so the drug would readily reach the tubercle bacilli. Thus the disease would be promtply cured before any significant destruction had occurred with no remaining potentialities from that particular infection.

Prevention

The only known efficacious method of preventing primary tuberculosis is to bar initial invasion with virulent tubercle bacilli or those of attenuated virulence. This is now being done with remarkable success over large geographical areas. The introduction into human or animal bodies of living tubercle bacilli of reduced

virulence produces primary tuberculosis with its accompanying allergy.

More Adults Than Children Now Acquire Primary Tuberculosis

Wherever tuberculosis is being successfully controlled by treatment and removal of contagious cases from their homes to institutions and the disease among domestic animals is also being eradicated, relatively few children develop primary tuberculosis (tuberculous infection). Soon most children enter adulthood uninfected. This situation was beginning to be apparent in Minnesota and a few other states a quarter of a century ago. As the years passed the number of children who developed primary tuberculosis (tuberculous infection) rapidly decreased until now the annual infection attack rate is only 0.3 per cent in cities and less in rural areas. Testing with tuberculin has revealed that this attack rate also obtains among adults. Therefore more adults now acquire primary tuberculosis (tuberculous infection) than children, as the period of adulthood is more than three times longer than that of childhood.

When it was determined that a preponderance of children were entering adulthood as nonreactors to tuberculin there was much speculation concerning the course tuberculosis takes when the primary type of disease (tuberculous infection) develops in adult life. It had long been theorized that primary disease acquired by adults would result in rapidly progressive and highly fatal forms of tuberculosis. It was questioned whether the programs of such organizations as the National Tuberculosis Association and the American Medical Association and of a large number of physicians in private practice which had been directed toward protecting infants and children against tubercle bacilli had been wrong. Moreover, there was opposition to the tuberculosis eradication program of the United States Bureau of Animal Industry which was depriving so many children of the bovine type of tubercle bacilli.

The theory was based upon the belief that primary tuberculosis (tuberculous infection) established in infancy or childhood resulted in dependable immunity which would be operative in adulthood, whereas the absence of such immunity would permit first infections occurring in adulthood to result disastrously.

Observations on Children and Adults

Beginning in 1920 and continuing to the present, we have had under observation more than 19,000 children and many thousand adults. Several hundred have been observed who first became reactors to tuberculin in adulthood. Many of them, particularly

students of nursing and medicine, were periodically tested with tuberculin every six to 12 months. Therefore the time when they became infected was determined with reasonable accuracy. We also saw a sizable group of persons who were periodically non-reactors to tuberculin before entering military service but who soon after separation were reactors. There was another group of older persons who became primarily infected under our observation.

When these adults developed primary tuberculosis (tuberculous infection) as manifested by the tuberculin reaction, they tolerated the invasion with tubercle bacilli in the same manner as the many children who were under our care. Most of the adults presented no abnormal chest x-ray film finding. A small percentage just as children presented shadow-casting parenchymal lesions and/or enlargement of hilum structures. Erythema nodosum occasionally appeared. Less evidence of pulmonary atelectasis was seen than in children, probably because of the larger caliber and greater rigidity of bronchi in adults. A few had fleeting symptoms such as moderate temperature elevation and malaise. The erythrocyte sedimentation rate was accelerated in some and normal in others. Over a period of many months to a year or so, the few shadow-

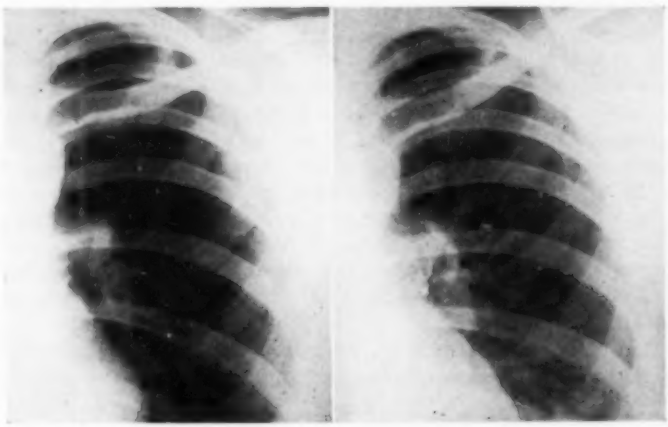

FIGURE 1a FIGURE 1b

Figure 1a: This woman did not react to tuberculin throughout a medical school course. While taking an internship she worked on a hospital tuberculosis service without strict contagious disease technic. About the time she became a reactor to tuberculin, x-ray film of her chest (December 20, 1943) revealed a shadow-casting lesion in the left lung near the periphery at the level of the second interspace, anteriorly. No significant symptom was present.—*Figure 1b:* Made from a film taken May 10, 1949, of same chest. Note residual lesion. No change had occurred through 1951.

casting lesions slowly resolved and in some, evidence of calcium deposits was later seen in lungs and hilum regions.

In our experience the theory pertaining to first infection with tubercle bacilli in adulthood being more destructive than infections occurring in childhood, proved to be a myth. In any large group of people, regardless of age, who have recently acquired primary tuberculosis which has sensitized the tissues, there will be a few whose lesions erode into lymphatic or blood vessels and so many tubercle bacilli reach the blood stream that generalized miliary disease ensues. Lesions located in or adjacent to the central nervous system may discharge large numbers of bacilli into ventricles of the brain or directly into the subarachnoid space and cause tuberculous meningitis. Foci may liberate their contents into bronchi, from which they are aspirated into finer ramifications and result in tuberculous pneumonia. Occasionally there is dissemination of tubercle bacilli from primary complex lesions directly into adjacent sensitized pulmonary tissue, resulting in tuberculous pneumonia.

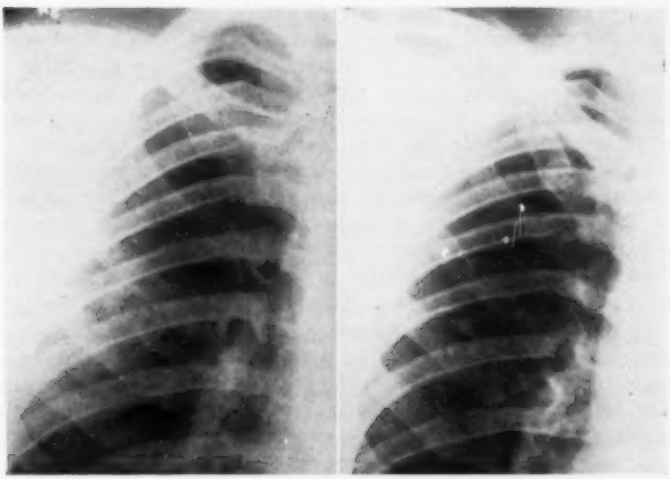

FIGURE 2a FIGURE 2b

Figure 2a: This man completed a medical school course as a nonreactor to tuberculin. During an internship he was assigned to a hospital tuberculosis service where strict contagious disease technic was not practiced. He became a reactor to tuberculin, and about the same time (December 4, 1943) a shadow-casting lesion was observed in the right lung at the level of the second, third and fourth interspaces, anteriorly. No significant symptom was present.—*Figure 2b:* Made from a film taken October 27, 1951, of same chest. Note small apparently calcified residual at level of the third interspace, anteriorly.

In a similar way acute pericarditis, pleuritis, peritonitis and synovitis result from primary foci appropriately located.

These acute conditions were long thought to represent primary tuberculosis because they were often the first recognized manifestations of the disease. Now it is known that they are reinfection forms of tuberculosis of endogenous origin. Whenever there has been an opportunity to administer tuberculin tests periodically, individuals with these conditions have nearly always become reactors before the acute episodes appeared.

Acute reinfection forms of tuberculosis developing soon after the tissues of our adults became sensitive to tuberculoprotein have been rare. Indeed, we have not seen a single case of meningitis or miliary disease among them. Occasionally acute exudative reinfection type of pulmonary lesions have occurred. Pleurisy with effusion has developed in a relatively small number.

Acute reinfection forms of tuberculosis have not appeared more frequently in our group first infected in adulthood than among our infected children.

Obviously, students who entered school as tuberculin reactors had foci of tubercle bacilli in various parts of their bodies which could at any time result in clinical disease. Thus it was to be expected that renal disease, epididymitis, bone and joint lesions and other extrathoracic clinical disease would appear among them, while the chest remained clear. Some of these we have seen. In others, two or more foci have become clinical almost simultaneously or at widely separated intervals. Some such lesions were in the lungs and others extrathoracically located. We have also seen such lesions develop remotely (two years or more) after students became infected while in school, but no more frequently or of any greater severity than those who entered school as reactors.

It has frequently been stated that students of nursing and medicine who became infected while in school developed much more tuberculosis than those who enter as reactors to tuberculin. The fact is overlooked that all reactors have tuberculous lesions whether they are sensitized before entering school or subsequently.

In such statements sight is lost of the fact that about the time allergy to tuberculoprotein is well established some individuals have allergic manifestations such as erythema nodosum, demonstrable pulmonary infiltrates and enlargement of hilum structures. When these were seen among adults recently infected but were not in evidence among those who entered as tuberculin reactors, the erroneous conclusion was drawn that more tuberculosis develops among those of the former group. Obviously those who entered school as reactors had already passed through these experiences.

Allergic manifestations had been present earlier in life. Both groups had the same experiences but at different times.

A few individuals, both children and adults, soon after allergy is established develop acute reinfection forms of tuberculosis, including pleurisy, pneumonia and, occasionally, meningitis and miliary disease. When these occurred more frequently among those who become infected as students than those who entered as reactors to tuberculin, it was again presumed that more tuberculosis developed among those of the former group. Sight was lost of the fact that among the groups from which the reactors on entrance were drawn, as many acute reinfections had occurred, but at an earlier age.

Among those students who entered school as reactors to tuberculin, only a few developed demonstrable tuberculous lesions. These were mostly chronic, slowly evolving processes. Obviously students who presented these lesions were outnumbered several times by those recently infected who developed allergic manifestations and acute reinfection forms of disease such as pleurisy with effusion.

Thus comparison of uncomparable situations and conditions may lead to the erroneous conclusion that less tuberculosis develops among persons infected in childhood than among those infected in adulthood. Diagnostic errors may play a considerable role in drawing erroneous conclusions. Far too much dependence has been placed upon x-ray shadows. In fact, shadows have been almost the sole diagnostic evidence in many instances despite the fact that they are never pathognomonic.

Among recently developed tuberculous lesions there is no way to differentiate between those of the primary and reinfection types except when one knows by actual testing about when the tissues became sensitive to tuberculin. Lesions which appear around that time are nearly always of the primary type, whereas, those which appear a few months later and subsequently are of the reinfection type. The presence or absence of enlargement of hilum structures as demonstrated by x-ray shadows associated with pulmonary lesions is inadequate, inasmuch as changes in the hilum region must be extreme and actually encroach upon the parenchuma before important shadows are in evidence. There are other conditions of the hilum region that cast x-ray shadows which may coexist with pulmonary tuberculosis. Moreover, markedly enlarged lymph nodes may be associated with reinfection type of pulmonary tuberculosis. Location is not dependable, since primary disease in adults may appear in any part of the lungs as in children. In our region, age does not help, since primary lesions develop more frequently in adults than in children.

When physicians came to look upon such shadow-casting lesions

in children as benign in most cases, a much more serious situation was thought to exist when identical appearing lesions were found in the chests of adults. Probably this is due to the former belief that tuberculous pulmonary lesions in adults are always of the reinfection clinical type, as all persons were thought to have acquired primary tuberculosis in childhood. Cases are still cited of young adults developing rapidly progressive primary disease. The question arises as to whether periodic tuberculin tests were administered with sufficient frequency to accurately determine when the first invasion occurred. If not, there is no way of knowing whether the lesions are of first or reinfection type.

One physician in a country where tuberculosis is still rife stated that 90 per cent of the students entering a university had been infected with tubercle bacilli in childhood. Each year a sizable number of clinical cases developed among the 12,000 students enrolled. Without factual data, it was his belief that all clinical cases had developed among the 10 per cent who entered school uninfected.

Our studies have revealed that after students become infected and the few allergic manifestations appear together with the occasional acute reinfection type of disease, their tuberculosis behaves just as that among students who reacted on entrance. All adult tuberculin reactors are potential cases of chronic reinfection types of tuberculosis and practically all such disease appears among reactors. This we have observed among not only students of nursing and medicine, but also among younger and older adults.

Veterinarians have shown that domestic animals, particularly cattle first infected in adulthood, do not develop any different form or more frequent progressive disease than those infected earlier in life.

Prevention of Primary Tuberculosis Among Adults

Prevention of primary tuberculosis in adulthood is as important but no more so than in childhood. It is accomplished in the two groups by the same method, namely, protecting against persons and animals with contagious disease. This necessitates finding and isolating all contagious cases and treating others to prevent contagion.

A special problem in prevention is encountered in students of nursing and medicine whose work brings them in contact with contagious cases of tuberculosis. Where little or nothing has been done to protect them a high percentage of those who enter as nonreactors to tuberculin develop primary tuberculosis complexes. In our School of Medicine over 65 per cent of nonreactors to

tuberculin on entrance in 1932 developed primary tuberculosis before graduation, while among those who entered as nonreactors in 1943, only 3.2 per cent had primary lesions on graduation. In one school of nursing 100 per cent of students who entered as nonreactors developed primary tuberculosis while in school prior to 1932, while among those who entered as nonreactors in 1942, none developed primary tuberculosis.

With these marked reductions in infection attack rate, there occurred corresponding decreases in morbidity. Prior to 1936, 4 to 10 per cent of the medical students developed demonstrable lesions or were ill before graduation. During the past eight years only one student had a demonstrable lesion evolve. He already had primary tuberculosis on entrance. In the school of nursing, 12 to 19 per cent of the students developed demonstrable lesions or were ill prior to 1936, but only two have presented clinical lesions in the past eight years. Both had primary tuberculosis before entering the school of nursing, as manifested by the tuberculin reaction.

Prior to this demonstration the belief was generally expressed that all students of nursing and medicine become infected or reinfected with tubercle bacilli before graduation. It was contended that no other situation is possible, since in line of duty they must come in contact with contagious cases of tuberculosis and could not be protected. Inasmuch as no report of a serious attempt to protect professional students against tubercle bacilli was found, it was decided to determine whether such an accomplishment was possible. Our method has consisted of simple, common sense fundamental procedures based on the knowledge that tuberculosis is contagious.

The procedures employed consist of: 1) Administration of the tuberculin test to every student on entrance to school and periodically testing those who did not react. 2) Making x-ray film inspection of the chests periodically of those who reacted to tuberculin on admission and those who subsequently became reactors. 3) Adequate examination for tuberculosis of all patients entering hospitals where students work. Those found to have contagious disease were immediately isolated and strict contagious disease technic was practiced. Students were withdrawn from hospitals which refused to employ such technic. 4) Requesting those in charge of postmortem rooms to afford protection of students, since tubercle bacilli remain alive long after the body is dead. 5) Impressing upon the students the contagiousness of tuberculosis and the necessity of their cooperation and participation in the program. 6) Pre-employment examination of all persons applying for work in hospitals. Examination of those already employed and periodic examinations thereafter.

There is still extant the fatalistic viewpoint that if professional students are protected against tubercle bacilli while in school, they will sooner or later be infected and reinfected after graduation. This depends largely upon the management of hospitals where they take internships and residencies. If these institutions have in effect or introduce a tuberculosis control program such as the above, there is no more reason why nurses and physicians should become infected than when they were in school. During the practice of their professions, nurses and physicians should demand that all hospitals in which they work provide the above protective measures. They must also exercise adequate precautions in examining and treating patients in homes and in their private offices.

In some areas of this country, except for those engaged in chest disease work many physicians are rarely in contact with contagious cases of tuberculosis. Legislators, the legal profession and insurance companies have come to the rescue by making tuberculosis compensable in a number of states. In such areas no hospital can afford to be without a program that will adequately protect personnel and patients against contagion.

In our area it now appears that in the near future practically all children will enter adulthood withou tthe hazard of tuberculous infections. Therefore, whatever primary infections occur in their generation will take place in adult life. This number should be extremely small. Already there are numerous schools in this state in which no child reacts to tuberculin. There are many counties where only 4 to 8 per cent of adults of 18 years have been infected with tubercle bacilli. Thus the situation is beginning to approach the ideal and already is in sharp contrast to the same area of three decades ago and with that now in parts of the world where nearly all children become infected and where throughout their adulthood clinical tuberculosis exists in epidemic form and where one-fourth to one-third of deaths from all causes are due to tuberculosis.

The accomplishments presented in this paper do not belong to any individual. They are the result of coordinated efforts of large numbers of persons, professional and otherwise, who set to work in the last decade of the 19th century and their program has continued to this moment. This report is not presented in the slightest spirit of boastfulness for there remains a tremendous amount of work before the eradication goal is attained. Moreover, there are nine other states, including Iowa, New Hampshire and Wisconsin, with less tuberculosis among their people. A sizable number of other states have almost as good records. It is significant that in all these states practically the same method of tuberculosis control has been employed.

This is the only method now known by which tuberculosis can be controlled and ultimately eradicated. Wherever it is introduced and pursued, its effectiveness is first in evidence among infants and young children who show a marked decrease in the incidence of tuberculin reactors with a corresponding decrease in morbidity and mortality when compared with those in the same community before the method was in effect. As the work progresses and these children attain older ages, including young adulthood, they show a much lower incidence of infection than those just ahead of them who were not so well protected in infancy and early childhood. In due time most children enter adulthood without primary tuberculosis (tuberculous infection) and they may so continue throughout the span of life if the tuberculosis control program is diligently executed.

Obviously in the absence of tubercle bacilli at any age there can be no infection, morbidity or mortality from tuberculosis. In this area it has been established to our complete satisfaction that tuberculous infections acquired in adulthood are no more hazardous than those in childhood. Therefore, the further into life's span primary tuberculosis can be prevented, the less time exists for clinical tuberculous lesions to mature and the sooner will the disease be eradicated from any community or nation.

SUMMARY

1) Primary tuberculosis develops in nearly all children in communities and nations where large numbers of persons with contagious tuberculosis remain in their homes and tuberculosis is prevalent among domestic animals.

2) The tuberculin reaction alone indicates the presence of primary tuberculous lesions. X-ray inspection of chests of children who have recently become allergic to tuberculoprotein rarely reveals the location of primary lesions in more than 5 to 8 per cent. The remainder are too small or not sufficiently dense, are in the 25 per cent of the lungs not visualized or are extrathoracically located.

3) Primary tuberculous lesions begin to develop in tissues that are not allergic to tuberculoprotein. Therefore the defense reactions are mild and nonspecific. The disease is usually benign. Symptoms, if present, are mild and fleeting. Occasionally lymph nodes and nodules draining primary pulmonary lesions become so enlarged as to extrinsically occlude bronchial ramifications. Again, exudate from the lesion or ulcerative foci in bronchial mucosa cause obstruction and atelectasis results.

4) As primary lesions develop, tissues of the body become sensitive to tuberculoprotein, which thereafter is a deadly poison to

them. Therefore, allergic tissues react in an intense and specific manner to invasions of tubercle bacilli. Lesions which develop in such tissues are of the reinfection or clinical type.

5) About the time allergy is established, erythema nodosum, pulmonary infiltrates and enlargement of hilum structures may be found in a small percentage of children. Soon thereafter the occasional child may develop acute reinfection type of tuberculosis such as pneumonia, miliary disease, meningitis, pleuritis, pericarditis and peritonitis. Later, chronic reinfection type of disease may appear extrathoracically, especially in bones and joints. Rarely does chronic reinfection type of pulmonary disease appear in children. However, among those infected in childhood this form of the disease begins to become manifest during adolescence and increases in frequency as age advances.

6) In this country primary tuberculosis develops more often in adults than in children, inasmuch as the infection attack rate is essentially the same in the two groups and since the period of adulthood is more than three time that of childhood.

7) Primary lesions which develop in adults are usually benign and present the same allergic manifestations in approximately the same proportion as in children. Atelectasis is less frequently seen in adults primarily infected, probably because of the larger size and more rigid walls of the bronchi.

8) Observations have revealed that the theory to the effect that primary tuberculosis in adulthood is a more serious disease than that acquired in childhood is untenable.

9) Since x-ray shadows are not pathognomonic, there is no possibility of differentiating between primary and reinfection type of lesions by the shadows they cast. Lesions which appear about the time tissues become sensitive to tuberculin are practically always primary, while those that appear months or years later represent reinfection type from endogenous or exogenous sources. The time when tissues become sensitive to tuberculoprotein is the determining factor in differential diagnosis.

10) The management of primary tuberculosis acquired by adults is no different than that of the child. All adults with primary tuberculosis, whether acquired in childhood or adulthood, are potential cases of acute and chronic reinfection forms of the disease and should be examined periodically and advised to report promptly if symptoms appear suggestive of meningitis, pneumonia, miliary disease, pleurisy, etc., in the intervals between regular examinations.

11) The only dependable method of preventing adults from acquiring primary tuberculosis consists of barring of tubercle bacilli from their bodies. Introduction of organisms of reduced virulence

produces primary lesions. Proper management of cases of tuberculosis and employment of strict contagious disease technic have proved to be efficacious.

RESUMEN

1) La tuberculosis primaria se desarrolla en casi todos los niños en los grupos humanos y en las naciones donde hay gran número de personas con tuberculosis en etapa contagiosa que permanecen en sus habitaciones y donde la tuberculosis prevalece entre los animales domésticos.

2) La reacción tuberculínica sola indica la presencia de lesiones de tuberculosis primaria. La inspección a los rayos X de los niños que se han tornado recientemente alérgicos a las tuberculoproteínas rara vez revela la ubicación de las lesiones primarias en mas del 5 al 8 por ciento. El resto de las lesiones son muy pequeñas o no suficientemente densas o bien estan incluídas en el 25 por ciento de los pulmones que escapan a la inspección o están situadas fuera del tórax.

3) Las lesiones tuberculosas primarias empiezan a desarrollarse en tejidos que no son alérgicos a las tuberculoproteínas. Por tanto las reacciones defensivas son moderadas y no específicas. La enfermedad es habitualmente benigna. Los síntomas, si los hay, son discretos y pasajeros. Ocasionalmente ganglios lifáticos y nódulos que canalizan de lesiones primarias crecen tanto que ocluyen extrínsecamente las ramas bronquiales. A su vez los exudados de la lesion o de los focos ulcerados en la mucosa bronquial causan obstrucción y la atelectasia resulta.

4) Mientras la lesion primaria se desarrolla los tejidos del organismo se tornan sensibles a la tuberculoproteína, que desde entonces se vuelve un veneno mortal para ellos. Por tanto, los tejidos alérgicos reaccionan de manera intensa y específica a la invasión de bacilos tuberculosos. Las lesiones que resarrollan en tales tejidos son del tipo de la reinfección o clínico.

5) Alrededor del tiempo que se establece la alergia pueden encontrarse en un porcentaje pequeño de niños el eritema nudoso, los infiltrados pulmonares y crecimiento de las estructuras hiliares. Pronto, después, alguno que otro niño puede desarrollar formas agudas de reinfección tales como la neumonía, la enfermedad miliar, meningitis, pleuritis, pericarditis y peritonitis. Después puede aparecer el tipo crónico de la reinfección extratorácica especialmente en los huesos y en las atriculaciones. Rara vez aparece la forma crónica pulmonar de reinfección en los niños. Sin embargo entre los infectados en la infancia esta forma de enfermedad empieza a manifestarse durante la adolescencia y su frecuencia aumenta a medida que avanzan en edad.

6) En este país la tuberculosis primaria se presenta mas a menudo en los adultos que en los niños puesto que siendo la proporción del ataque el mismo en las dos edades el periodo de la vida adulta es mas de tres veces mayor que el de la infancia.

7) Las lesiones primarias que se desarrollan en los adultos son generalmente benignas y presentan las mismas manifestaciones alérgicas en la misma proporción aproximada que los niños. La atelectasia es menos frecuente en los adultos con primoinfección probablemente debido al mayor tamaño y a la mayor rigidez de la paredes bronquiales.

8) La observación ha revelado que la teoría de que la primoinfección en el adulto es mas grave que en el niño, es insostenible.

9) Puesto que las sombras a los rayos X no son patognomónicas, no hay posibilidad de diferenciar entre las formas de primoinfección y de reinfección por las manchas que ambas producen. Las lesiones que aparacen alrededor del tiempo que los tejidos se vuelven sensibles a la tuberculina son practicamente siempre primarias en tanto que las que aparecen meses o años después representan el tipo de la reinfección de fuente endógena o exógena. El tiempo cuando los tejidos se vuelven sensibles a la tuberculoproteína es el factor determinante en el diagnóstico diferencial.

10) El tratamiento de la tuberculosis primaria adquirida en la edad adulta no es diferente del de los niños. Todos los adultos con tuberculosis primaria ya sea adquirida en la infancia o en la edad adulta, son casos potenciales de reinfección aguda y crónica de la enfermedad y deben ser examinados periódicamente y aconsejados que se presenten si aparecen síntomas sugestivos de meningitis, neumonía, enfermedad miliar, pleuresía, etc., en los intervalos de los exámenes.

11) El único método seguro para evitar que los adultos adquieran la tuberculosis primaria consiste en excluir los bacilos del organismo de ellos. La introducción de gérmenes de virulencia disminuida produce lesiones primarias. La adecuada atención de los casos de tuberculosis y el empleo de la estricta técnica de las enfermedades contagiosas ha demostrado ser eficaz.

RESUME

1) La primo-infection tuberculeuse frappe approximativement tous les enfants dans les collectivités et les nations où les personnes atteintes de tuberculose contagieuse restent chez elles, et où la tuberculose est fréquente chez les animaux domestiques.

2) Les réactions tuberculiniques à elles seules indiquent l'existence d'une primo-infection tuberculeuse. L'examen radiologique du thorax des enfants qui ont récemment viré leur cuti-réaction montre rarement les lésions primaires dans plus de 5 à 8% des cas.

Pour les autres, il s'agit de lésions trop petites ou n'ayant pas de densité suffisante pour être visible ou bien il s'agit de localisations extra-thoraciques.

3) Les lésions de primo-infection se développent tout d'abord dans les tissus qui ne sont pas sensibles à la tuberculine. Il en résulte que les réactions de défense sont faibles, et non spécifiques. L'affection est généralement bénigne. S'il y a des symptômes, ils sont discrets et peu nets. Dans certains cas, les ganglions lymphatiques drainant les lésions pulmonaires de primo-infection prennent une telle importance qu'ils réalisent une occlusion bronchique extrinsèque. Des mucosités bronchiques provenant de lésions sécrétantes ou même de foyers ulcérés sont cause d'obstruction bronchique et peuvent déterminer une atélectasie.

4) A partir du moment où les lésions primaires sont apparues, les tissus deviennent sensibles à la tuberculine. Cette substance réalise pour eux un poison mortel. C'est ainsi que les tissus allergiques répondent de façon intense et spécifique aux invasions des bacilles tuberculeux. Les lésions qui se développent alors ont les caractères de lésions de réinfection.

5) C'est à peu près au moment où apparait l'allergie que les enfants, dans une petite proportion, peuvent être atteints d'érythème noueux, d'infiltrats pulmonaires, et d'augmentation des hiles. Peu de temps après, on peut constater chez l'enfant des formes de réinfection tuberculeuse, telles que pneumonie, tuberculose miliaire, méningite, pleurésie, péricardite et péritonite. Plus tard, on peut assister à l'apparition d'une tuberculose chronique à type de réinfection se localisant en dehors du thorax, et plus particulièrement sur les os et les articulations. Il est rare que les enfants soient atteints de tuberculose chronique à type de réinfection. Toutefois, chez les individus qui ont été infectés au cours de leur enfance, cette forme de tuberculose commence à se manifester au cours de l'adolescence et augmente en fréquence à mesure que l'âge avance.

6) Dans ce pays, on constata plus souvent des primo-infections chez des adultes que chez des enfants. Ceci semble s'expliquer par le fait que la proportion des atteintes étant la même dans les deux groupes, la période de l'enfance est trois fois moins longue que la période de lâge adulte.

7) Les lésions primaires, quand elles surviennent chez des adultes sont généralement bénignes, et présentent les mêmes manifestations allergiques que chez l'enfant. Chez les adultes qui viennent d'avoir une primo-infection, l'atélectasie est moins fréquente, vraisemblablement à cause de la plus grande dimension des bronches et de la rigidité de leurs parois.

8) Les observations montrent qu'il est impossible de soutenir

que la primo-infection à l'âge adulte réalise une affection plus grave que celle de l'enfance.

9) Etant donné que les ombres radiologiques n'ont rien de pathognomonique, il n'y a pas de possibilité de différencier radiologiquement les lésions de primo-infection, et celles de réinfection. Les altérations qui apparaissen à tpeu près en même temps que l'allergie tuberculinique sont pratiquement toujours dues à une primo-infection. Celles qui apparaissent des mois ou des années plus tard sont dues à des réinfections, soit endogènes, soit exogènes. Le facteur déterminant pour le diagnostic différentiel entre primo-infection et réinfection est donné par le moment où apparait la sensibilité tuberculinique.

10) La conduite à tenir en présence d'une primo-infection survenant chez un aduite n'est pas différente de celle qu'on doit avoir lorsqu'il s'agit d'enfants. Tous les adultes qui ont eu une primo-infection, soit au cours de leur enfance, soit plus tard, sont sous la menace de réinfection à forme aigue ou chronique. Ils devraient être examinés périodiquement, et même dans les intervalles des examens systématiques si des symptômes apparaissent, qui peuvent faire craindre une méningite, une pneumonie, une tuberculose miliaire, une pleurésie, etc.

11) La seule méthode efficace pour prévenir l'apparition d'une primo-infection tuberculeuse chez l'adulte consiste à éliminer les bacilles tuberculeux de leur organisme. L'introduction de bacilles de virulence atténuée détermine des lésions de primo-infection. Les soins qualifiés appliqués à la tuberculose pulmonaire, et les techniques d'élimination formelle de toute possibilité de contagion ont donné la preuve de leur efficacité.

Practical Significance of Tuberculous Infection with Streptomycin-Resistant Organisms*

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Streptomycin had been in use for nearly three years, when the first two cases of tuberculous infection with streptomycin-resistant organisms were reported in patients who had not received previous chemotherapy. One of them was the case[1] of a Navy nurse who was tuberculin negative before she was assigned to the streptomycin study unit of a naval hospital. She took care of patients whose bacilli became resistant to streptomycin. Subsequently she developed a tuberculous lesion and her organisms showed growth on media containing 1000 mcgm. of streptomycin per cc. The other case[2] was that of a colored hospital attendant in a Veterans Hospital at Washington, D. C., who developed pleural effusion, and the organisms recovered from the fluid showed an initial resistance to 100 mcgm. of streptomycin per cc. Shortly thereafter, the third case[3] was reported from our hospital; this was a 22-year old white male attendant who was tuberculin negative when he was assigned to a ward where he was exposed to at least 16 streptomycin-resistant cases. He left his job after four months, and two months later he developed chills, high fever, and pleural effusion; organisms could not be recovered from the sputum or pleural fluid, but two urine cultures were positive and the bacilli proved to be resistant to streptomycin in a concentration of 100 mcgm. per cc. A few months later, shortly before he died with wide-spread disease in all of his organs, the mycobacteria recovered from his sputum showed the same high resistance. The fourth case[4] was reported from Cornell University; this was a nurse whose tuberculin test was already positive when she entered nursing school. She took care of several streptomycin-resistant cases and when subsequently she developed tuberculosis, her organisms showed growth on media containing 1000 mcgm. of streptomycin per cc. The fifth case,[5] reported from Great Britain, was that of an 11-week old infant with miliary tuberculosis in whose gastric lavage highly resistant

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micro-organisms were found. The mother's disease was discovered on the 18th day after delivery, at which time the infant was separated from her. The mother's sputa were negative and she never received streptomycin; it was therefore assumed that she was infected with streptomycin-resistant organisms, and transmitted them to her child. The sixth case,[6] reported from France, was that of a woman infected by her streptomycin-treated husband; the seventh,[7] that of a woman living with a patient harboring streptomycin-resistant bacilli, and the eighth,[8] also from France, was apparently a laboratory infection occurring in a female student.

In the July and October 1951 Quarterly Progress Reports of the Veterans Administration Chemotherapy Study Units, four additional cases were described. The ninth and tenth cases[9] were colored attendants of the Veterans Hospital, Oteen, North Carolina, whose clinical course was rather unfavorable. The eleventh,[10] from Veterans Hospital, Butler, Pennsylvania, was that of a previously tuberculin positive dentist whose mycobacteria—in contradistinction to those of his brother who simultaneously developed tuberculosis—were found to be moderately resistant to streptomycin. The twelfth case,[11] from Veterans Hospital, Alexandria, Louisiana, was that of a former Veterans Administration employee who had no known contact with tuberculosis before becoming ill, and whose lung lesion reacted well to collapse treatment without antibiotics; however, when he later developed genito-urinary symptoms, the organisms recovered from the urine were found to be streptomycin-resistant.

Since February 1947, when streptomycin therapy was started at the Veterans Hospital, Walla Walla, Washington, in addition to case 3, three more employees have developed tuberculosis. One was a nurse who had pleural effusion from which no mycobacteria could be recovered; the others, a physician and an x-ray technician, both long-time employees whose assignments have not changed, who did not have any intercurrent diseases or changes in their favorable financial or family situation, and in whose cases the only environmental change was their exposure to streptomycin-resistant patients, had, nevertheless, entirely sensitive organisms in their sputa.

Recently, in this hospital, a 53-year old laboratory technician who had been doing sputum examinations, and whose tuberculin test was positive several years before, developed a cold, and had residual cough and expectoration. One sputum smear and one culture were found to be positive, and the mycobacteria grown on this culture showed moderate resistance to both streptomycin and PAS. This man had a normal chest x-ray film, and bronchoscopy

failed to reveal endobronchial disease. He was discharged to duty after a four-month period of observation, during which his x-ray film, sputa, and gastrics remained negative.

Nine out of these 13 cases were hospital employees exposed to streptomycin-resistant patients. Some of them occurred in persons who were tuberculin negative and some had positive tuberculin tests prior to development of their tuberculosis. There is no complete information available concerning the clinical courses of all of these individuals. Four of them seemed to have been doing poorly; whether this has anything to do with streptomycin-resistance of the organisms, is questionable. Cases three and five might have been saved if the bacilli had been sensitive; a short course of streptomycin in the terminal stage of case three was of no avail.

We were interested to learn whether streptomycin-resistant patients could superinfect their room mates who had no streptomycin treatment. Superinfection unquestionably does occur. A case[12] of superinfection in a sanatorium was clearly demonstrated when a patient with tuberculosis caused by the human type of bacilli was subsequently infected with the bovine mycobacteria of his room mate. This is a rare occurrence, and, now, streptomycin seems to prove on a large scale that the role of superinfection in tuberculosis is rather insignificant. Our streptomycin-sensitive cases have never been separated from the streptomycin-resistant patients, nevertheless there was no incidence of initial resistance to streptomycin in more than 400 cases, although many of these patients had been exposed to cross infection from streptomycin-resistant room mates for a long period of time prior to their treatment with the drug. In addition, repeated resistance studies were made on five of our "good chronics" who have never received streptomycin but shared small rooms with resistant cases for long periods of time. All five have had sensitive organisms consistently. It seems, therefore, that the problem of spread from case to case in tuberculosis hospitals has no practical significance. Recently, there was a preliminary report from the Veterans Hospital, Castle Point, New York,[13] which was at variance with our experience. Patients who had been in that hospital without chemotherapy for four or five years, did show an occasional resistant culture among many sensitives on repeated examination.

After five years of rather extensive use of the drug, the discovery of only 13 cases makes the problem appear to be of negligible importance. One must, however, assume that there are many more of these cases which have not been recognized because streptomycin sensitivity tests have not, as yet, been performed on a large scale. The primarily exposed hospital personnel has to be protected through enforcement of contagious technique. The transmission

of streptomycin-resistant mycobacteria may eventually become a major health hazard, especially now, when there is a definite tendency toward the use of prolonged streptomycin courses,—for one year or longer. According to a preliminary report from Veterans Hospital, Sunmount, New York,[14] prolonged streptomycin courses may result in the loss of viability of the mycobacteria. If this proves to be true, the entire problem of transmission of streptomycin-resistant organisms can be disregarded. If, however, prolonged courses result in increased number of streptomycin-resistant cases, this will increase the public health hazard of transmission of streptomycin-resistant bacilli.

For proper evaluation of the practical significance of this problem, the following factors have to be considered: (1) Addition of PAS to streptomycin decreases emergence of streptomycin-resistance in a 120-day course of treatment from about 70 per cent to less than 10 per cent, and the latter figure is still lower when streptomycin is being used twice weekly. (2) Cavitary cases are more liable to develop resistance. A review of 80 resistant cases in this hospital revealed that 82 per cent had cavitary disease. (3) Whereas, formerly, streptomycin-resistance was believed to be permanent, we now know that, in a number of cases, resistant bacilli are replaced by sensitive ones after a period of time. (4) The clinical criteria of resistance have changed; whereas formerly it was believed that no clinical response to streptomycin could be anticipated if there is even the slightest growth at 10 mcgm. per cc., now even a minimal inhibition of growth at 100 mcgm., on comparison with the control, is being accepted as evidence of sensitivity. (5) It is known that the degree of sensitivity varies, in some cases, in the different organs or even different parts of the same organ. (6) In a number of completely streptomycin-resistant cases, there seems to be some, although usually not dramatic, clinical response to a combined streptomycin and PAS regimen.

The available evidence which has been recited leads the author to the following tentative conclusions: The public health aspect of transmission of streptomycin-resistant mycobacteria appears to be serious enough to withhold this treatment from the irresponsible patient who is likely to leave the hospital irregularly, especially if he has cavitary disease. These patients should only be given short emergency courses. On the other hand, it does not seem to represent a serious enough reason to withhold streptomycin therapy from any other active cases of tuberculosis in which there is clinical indication for such treatment. This group includes minimal active cases and "idiopathic" pleural effusions in which the use of streptomycin is still a controversial issue, but in which emergence of

resistance to this drug is unlikely, especially if it is given twice a week with PAS, 12 grams daily.

Addendum

Following presentation of this paper, an article[15] reporting two more such cases came to the author's attention. This raises the number of known initially resistant cases to 15.

SUMMARY

A new case of tuberculous infection with streptomycin-resistant organisms is reported. Only the irresponsible patient with a history of many irregular discharges provides a public health hazard by transmission of streptomycin-resistant mycobacteria; otherwise, the potential danger of spreading streptomycin-resistant strains does not seem to be a factor of sufficient practical importance to withhold streptomycin from any active case of tuberculosis, including the minimal and the "idiopathic" pleural effusion cases. In tuberculosis hospitals, transmission of resistant bacilli from one patient to another is practically non-existent; therefore, there is no need of separating streptomycin-resistant cases from those with sensitive organisms on the wards. Hospital personnel should be protected by strict contagious technique.

RESUMEN

Se refiere un nuevo caso de infección tuberculosa con gérmenes estreptomicino-resistentes. Solamente el enfermo irresponsable con historia de muchas salidas de hospital irregularmente, significa un peligro para la salubridad pública por la transmisión de micobacterias estreptomicino-resistentes. Por lo demás el peligro potencial de la diseminación de bacilos estreptomicino-resistentes no parece ser un factor de importancia practica suficiente para dejar de proporcionar la estreptomicina a todo caso activo de tuberculosis incluyendo los casos "mínimos" y los derrames pleurales "idiopáticos." En los hospitales de tuberculosos la transmisión de bacilos resistentes de un enfermo a otro practicamente no existe; por tanto no hay necesidad de separar los casos de estreptomicino-resistentes de los sensibles en las salas. El personal del hospital debe ser protegido por una técnica estricta de enfermedades contagiosas.

RESUME

Un nouveau cas d'infection tuberculeuse à germes streptomycino-résistants est rapporté. Le danger de propager des souches streptomycino-résistantes ne semble pas un facteur d'importance pratique suffisante pour éviter l'usage de l'antibiotique dans tout cas de tuberculose active, même dans ceux où il ne s'agit que d'une

atteinte pulmonaire discrète ou d'une simple pleurésie séro-fibrineuse. Dans les services hospitaliers de tuberculeux, la transmission des bacilles résistants d'un malade à l'autre est pratiquement inexistante. Il n'y a donc aucune raison de séparer les malades devenus streptomycino-résistants de ceux qui sont restés sensibles. Le personnel hospitalier doit être protégé par les moyens stricts habituels.

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Recovery of Pulmonary Function After Crushing Injuries of the Chest*

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Thoracic injuries may be best divided into two major groups, depending upon whether a wound through the chest wall has occurred. These groups are usually termed "penetrating" or "non-penetrating" injuries. The penetrating wounds are subdivided into "closed penetrations" and "sucking wounds." Non-penetrating contusions are best termed "crushing injuries of the chest" and divided into those which produce instability of the chest wall and those which only result in impairment of motion.

This classification of chest injuries has obvious clinical importance for a penetrating wound of the chest presents the hazards of bacterial contamination, pneumothorax, and puncture-type injury of the lung, heart, and great vessels. Sucking wounds present a unique problem. If they are of any size, pulmonary ventilation is extremely difficult or impossible. Prompt closure is a surgical emergency of the highest order. Crushing injuries, on the other hand, do not threaten the heart or major vessels with puncture. However, extensive contusion and laceration of the lung and intercostal arteries by sharp rib fragments results in widespread hemorrhage into chest wall and lung. Pulmonary edema often develops rapidly, and air leakage from the lung may produce pneumothorax and subcutaneous emphysema. Contusion of the myocardium is a well recognized entity. These injuries, moreover, result in severe respiratory embarrassment by interference with chest wall motion.

The various aspects of the management of thoracic injuries defined by this classification have been well covered in the surgical literature of the last 30 years, and there is little nourishment to be gained from a review of the various technical methods of how best to handle a sucking wound of the chest or a stab wound of the heart or any of the other well understood and commonly recognized anatomical disruptions which occur. Consideration of

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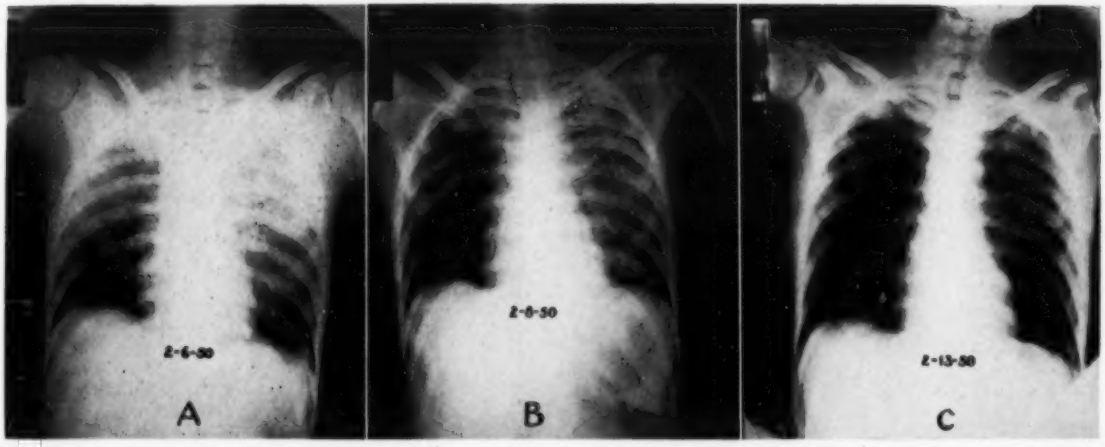

FIGURE 2: (A) Roentgenogram of chest of 26-year old nurse 30 minutes after sustaining crushing injury of chest. No ribs fractured, no hemorrhage into lungs. Bilateral upper lung field densities due to pulmonary edema (traumatic wet lung). Patient anoxic, cyanotic, disoriented, with frothy serous fluid welling into pharynx.—(B) Good clearing in two days with six hours' initial positive pressure oxygen followed by oronasal oxygen by catheter for 24 hours.—(C) One week later complete clearing of lung fields.

the basic disturbances in physiology of respiration and circulation which occur as a result of thoracic injury is more rewarding. These changes are common to both groups but are most clearly apparent in crushing injuries, which are also by far the most frequent in civilian practice.

Dr. Newell Wood[1] working in our group at the U. S. Veterans Hospital in Minneapolis has made a rather surprising observation in people with minimal injuries to the chest. Using the technique of differential bronchospirometry he has demonstrated that following the fracture of a single rib without any evidence of parenchymal or pleural damage by physical examination or roentgenogram and with little reduction in tidal air on the injured side there is a marked reduction in oxygen absorption on that side. Figure 1 illustrates these changes, showing both the normal volume of tidal air and the marked reduction in the oxygen absorption. Thus, it seems apparent that following even minor injury to the chest wall some change occurs in the flow of blood through the lung which seriously cripples it as an organ of respiration.

Crushing injury of the chest, even though not accompanied by fractured ribs or sternum, may result in severe acute pulmonary

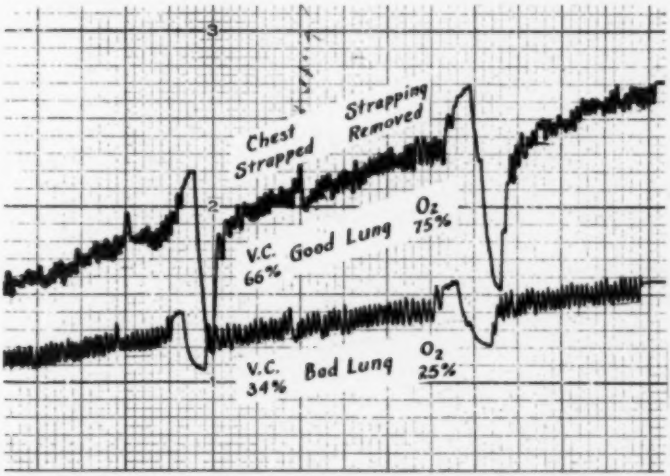

FIGURE 1: Differential bronchospirometry tracings of young male with minor crushing injury of chest, only one rib fractured. Note that tidal air and minute volume are the same on both sides, but vital capacity and oxygen uptake are greatly diminished on injured side. Chest strapping has no effect on normal exchange where only one side is injured and is not flail.

edema.[4] The roentgenograms shown in Figure 2 illustrate acute pulmonary edema developing in a 26 year old nurse within 30 minutes after she sustained a severe crushing injury which fractured her clavicle, contused her chest, but failed to fracture her ribs. On admission to the hospital soon after the accident she was deeply cyanotic, restless, and irrational from anoxia. She was in moderate shock and expectorating large amounts of frothy serous fluid which welled into her pharynx. Electorcardiograms obtained at this time and serially afterwards demonstrated no cardiac injury, and with adequate treatment, to be discussed later, she promptly responded and the edema cleared.

Such a rapid accumulation of serum in the lungs probably comes about as a result of the changes demonstrated by Wood's studies mentioned above. As a result of severe bilateral contusion with painful splinting of the intercostal musculature the ventilation of both lungs is sharply reduced, and concomitant with this comes a reduction in circulation through the lungs brought about by closure of the vascular bed surrounding the poorly ventilated alveoli. This results in acute pulmonary hypertension with transudation of fluid from the circulation into the lung. Cournand[2] and others have shown that marked pulmonary hypertension may be produced in the normal individual by a reduction in the amount of oxygen in the alveoli. Antedating Cournand's observations by several years are Drinker's[3] classical studies on the production of pulmonary edema in dogs by anoxia. This same type of pulmonary edema frequently develops after severe head injuries which result in respiratory inadequacy on a neurogenic basis.

Differential bronchospirometric studies following the induction of pneumothorax demonstrate that with moderate to advanced collapse of a lung there occurs simultaneously with the reduction in ventilatory efficiency of the organ a reduction in the perfusion of its alveoli. This common and obvious clinical observation has been made by all of us who are familiar with patients having therapeutic pneumothorax established, for were not the amount of blood perfusing through a lung nicely adjusted to its ventilation every patient carrying a sizeable pneumothorax would show a persistent arterial oxygen unsaturation with the resultant development of polycythemia and cyanosis. If, however, the pulmonary collapse is accompanied by loss of efficient ventilatory motions of the diaphragm and chest wall due to reflex splinting either from pain or pleural irritation, the reduction in profusion will be much greater as it will match the reduction in ventilation. It is thus apparent that collapse of a lung, even though incomplete, by the collection of air, serum, or blood within the pleural space following thoracic injury compounds the difficulties and leads to serious

respiratory difficulties. The embarrassment is of a much greater degree than one familiar with the capacity of a patient carrying a sizeable pneumothorax would anticipate.

As we have seen from the foregoing observations, serious contusion of the chest wall with bruising and disruption of the intercostal musculature will result in marked reduction in ventilation and perfusion of the lung with serious embarrassment of respiration. If sufficiently severe, it may result in fatal or near fatal pulmonary edema. If complicated by pleural effusion or pneumothorax or contusion of the myocardium, a prompt fatality may easily ensue without the fracture of a single rib or the penetration of a millimeter of skin by any foreign object. The victim of such an injury, however, rarely escapes without multiple rib fractures occurring both posteriorly and anteriorly in the arc of the rib. Loss of the architectural integrity of the thorax and paradoxical motion of the chest wall result. Pendulum respiration now occurs, as illustrated in Figure 3. The patient when supine and viewed from the foot of the bed presents the picture of the thorax swinging toward the more intact side on inspiration and back to the unstable side on expiration. Efficient ventilation is

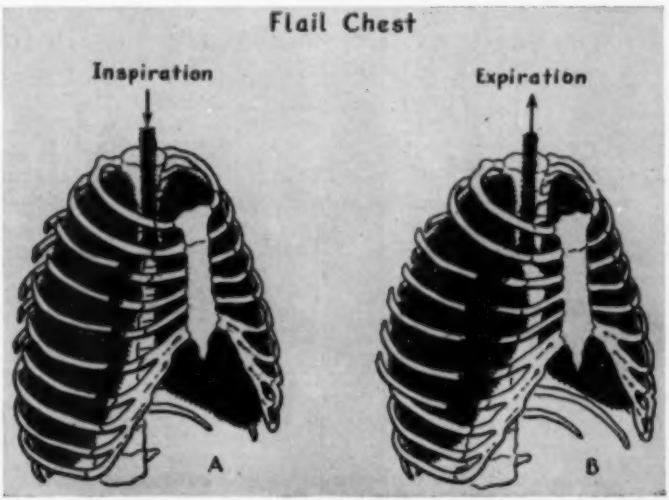

FIGURE 3: Artist's sketch showing "caving in" effect on inhalation (A), and "bulging out" on exhalation (B), of flail chest wall produced by multiple rib fractures. This is "paradoxical respiration." Note reduction in size of lung on injured side on inspiration and enlargement on expiration in paradox to the sound side. As a result, air is exchanged between the two lungs rather than being moved in and out the trachea. Alveolar ventilation is greatly impaired.

impossible as a great proportion of the air motion produced by this type of respiration is simply to and fro from one lung to the other. Pulmonary hypertension and edema promptly result from the anoxia of the failing ventilation and further compound the difficulty. It is only because of the tremendous respiratory reserve with which the average individual is equipped that this type of injury can be tolerated long enough for him to reach a hospital.

Reflex splinting of the chest wall due to pain and muscle spasm with its resultant shallow respiration and suppression of cough rapidly allows the collection of bronchial secretions. With loss of stability of the chest wall and the development of paradoxical respiration, effective coughing is impossible (Figure 4). Frequently with injuries of this severity contusion of the lung occurs with hemorrhage into the tracheobronchial tree and the formation of clots. Bronchial obstruction from thick retained secretions and blood clots may rapidly develop. It takes little to drown such a patient.

Treatment

From the standpoint of immediate treatment, patients sustaining crushing injuries of the chest may be divided into two groups.

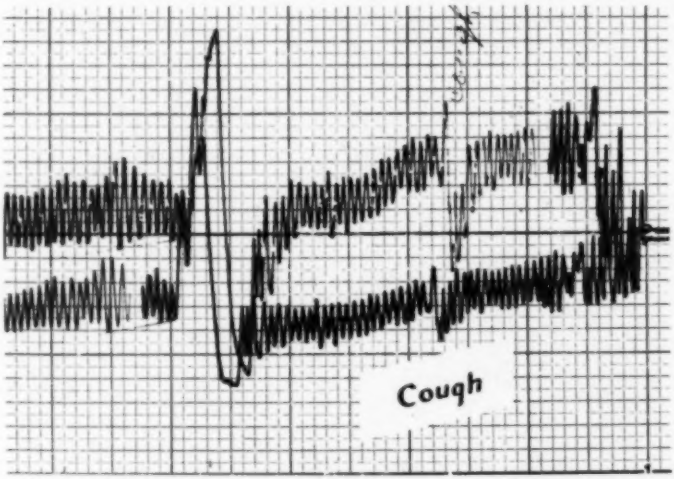

FIGURE 4: Differential bronchospirometric tracings. Minor crushing injury, unilateral. Note that again as in Figure 1 minute volume and tidal air are the same on the two sides, but the oxygen uptake is greatly diminished on the injured side. Coughing results in good air expulsion by the uninjured side with no effective air motion on the injured side (lower tracing). If injury is severe enough to produce paradoxical motion, coughing is impossible on both sides.

If the injury has been such that the loss of pulmonary function is still within physiologically tolerable limits the clinical management need concentrate on only those procedures which are necessary to prevent further respiratory embarrassment. However, if the injury is of such magnitude as to produce anoxia, dyspnea, and rapid respiration, immediate steps must be taken to recover and maintain adequate pulmonary function.

The first group of patients, in spite of their painful injuries and difficult respiration, will be able to maintain adequate ventilatory exchange if their chest walls are stable and they have good diaphragmatic motion. Immediate pleural complications will be absent although pleural effusion may occur later and must be watched for. Hemorrhage into the lung will be slight, if present at all, and pulmonary edema minimal, with the result that the initial airway will be quite adequate. This patient will be awake, rational, and co-operative. He will usually distinguish himself by his persistent and bitter complaints of painful respiration. The fact that he talks a great deal is a good omen but may lead to his later undoing.

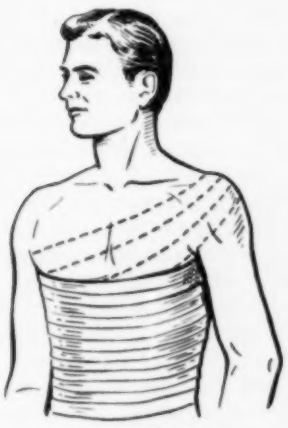

FIGURE 5

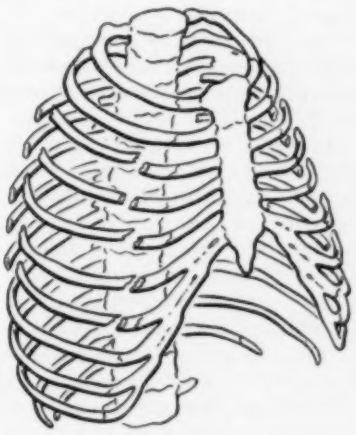

FIGURE 6

Figure 5: Chest Stabilized by Strapping. Scheme of chest strapping for unilateral injuries. Skin should first be coated with tincture of benzoin and tape should be applied in strips completely encircling thorax if necessary to control paradoxical motion. High injuries can be stabilized by strapping across to contralateral shoulder.—*Figure 6:* Artist's sketch showing rib fractures which result in bilateral loss of stability of chest wall. Circumferential strapping will not control a bilateral flail chest without very serious loss of pulmonary ventilation. Note lowest ribs and upper two are still intact though fissured; otherwise, sternum would also be flail. (See Figure 7).

The treatment of this patient may be rather simply accomplished. Partial immobilization of the chest wall by circumferential bandaging or adhesive strapping will relieve a great deal of the pain of respiration and may permit fairly effective coughing (Figure 5). Elevation of the head of the bed to 45 degrees will make respiration easier as it encourages diaphragmatic motion. Medium concentration oxygen therapy, such as can be obtained with a good tent or an oronasal oxygen catheter, will be good insurance against anoxic pulmonary edema and will provide the patient additional comfort by lessening his ventilatory requirement somewhat.

The gradual accumulation of tracheobronchial secretions due to inhibition of the cough reflex by pain is the major hazard this patient faces (Figure 4). Many such a patient has been allowed to comfortably and quietly drown while he and his attendants serenely assumed all to be well. This happens because a sedated patient at bed rest with painful shallow respiration may progressively lose pulmonary function by creeping atelectasis without showing any symptoms. The atelectasis advances until the vital capacity is diminished to the point where it approaches tidal air. Then any exertion, such as talking, coughing, or turning will immediately produce an oxygen debt and carbon dioxide build-up which cannot be compensated for. Hyperpnea results, increasing the oxygen debt; anoxic restlessness quickly follows and further compounds the difficulties. Death is sudden. We are usually informed of such disasters by a rather mystified nurse or interne who lamely explains that "Mr. Jones had a good night and seemed perfectly all right this morning when I took his tray in, but when I went back to the room a few minutes later he was dead." A glance at the chart reveals that Mr. Jones' bitter complaints of chest pain were instrumental in his demise as he talked his attendants out of a couple of morphine hypos and a little pentobarbital with the plea that he had to get some sleep. Later, since he was sleeping so nicely, nobody had the heart to rouse him and put him through the agony of coughing.

The poppy derivatives and the barbital compounds are one of the biggest hazards this patient faces. Some pain relief is needed—but an eighth of morphine or a sixth of a grain of pantopon is as big a dose as can safely be given a chest injury. Larger doses will abolish the cough reflex. The barbital compounds are equally hazardous as they also abolish the cough reflex and numb the respiratory center. They must be carefully avoided. Fifteen to 20 grains of chloral hydrate by rectum is all that can be given safely. If a skilled surgeon or anesthetist is available who can safely block the intercostal nerves with procaine, this is the best type

of pain relief available. It should be remembered, however, that this is one of the easiest ways to produce an accidental pneumothorax which may only compound the difficulties.

Tracheobronchial aspiration by a catheter passed through the nose into the pharynx, and then advanced through the larynx on inspiration is extremely valuable in these patients. The irritation of the trachea by the catheter will produce effective coughing, and the loosened sputum is immediately evacuated by suction, clearing the airway quite efficiently. The violent coughing stimulated by this maneuver also results in deep, effective inspiration with aeration of atelectatic pulmonary segments. With a little determination, even the inexperienced can readily get a catheter into the trachea by this maneuver and do quite an effective job. One should not wait until the chest is filled with rhonchi and atelectasis is well advanced to start catheter aspiration of the tracheobronchial tree; rather, the procedure should be carried out on a prophylactic basis. Aspiration should be done two or three times a day, and each time it should be persisted in until the patient is unable to raise any more sputum and his breath sounds are clear of moisture. The procedure should be continued on subsequent days until the patient is able to take over and remove his own tracheobronchial secretions by effective cough. It is helpful to explain to the patient that if he finds it possible to really settle down and cough up his sputum this highly distasteful procedure can be abandoned.

The other complications to which one must be alert in this type of patient are pleural and cardiac. Delayed pleural effusion may develop slowly over several days to a week after injury. A small amount of intrapleural blood as it begins to hemolyze may stimulate considerable effusion in certain patients. Mediastinal and subpleural hematomas likewise stimulate pleural effusion. Occasionally, sufficient pneumonitis develops in the atelectatic areas of the lung that an inflammatory pleural exudate collects. These are not common since the advent of antibiotics, and when they do occur they are usually sterile. All such pleural effusions have a tendency to clot, and before this occurs they should be aspirated completely dry and the pleural space kept dry by as frequent aspirations as are required to accomplish this end. It is well to remember that these effusions are much more likely to clot than they are to reabsorb and that the only way they can be handled after clotting is by open thoracotomy and decortication of the lung. Spontaneous pneumothorax occasionally occurs several days after a reasonably minimal chest injury and is probably related to the tearing of the lung by an old adhesion or to the rupture of an emphysematous bleb due to the increase in intrapleural

pressure which comes about with bronchial obstruction and atelectatic collapse of a portion of the lung. Overexpansion of the remaining lung occurs, and if blebs are present they may well rupture under these circumstances. It it well to keep this complication in mind and to watch the patient carefully for its development during the first 10 days to two weeks after the injury.

Myocardial bruising may occur with seemingly minor chest injuries, and initially the cardiac difficulties may be obscured by the respiratory difficulties. For this reason, it is well to get admission electrocardiograms on all patients who have sustained thoracic injury. Occasionally a patient showing electrocardiographic evidence of myocardial contusion dies suddenly hours to days after injury, presumably from ventricular fibrillation. Probably the best prophylactic management for this type of patient is to make certain of excellent oxygenation at all times.

Severe crushing injuries of the chest result in loss of stability of the chest wall. This comes about as a result of fracture of many ribs at two or more points along the arc of each rib. It may be unilateral as in Figure 3 or bilateral as in Figure 6. Paradoxical motion of the chest wall results and interferes greatly with adequate ventilatory exchange.

Contusion and rupture of the lung is frequent and results in hemorrhage into the lung, pulmonary edema, both from the direct result of the injury and the anoxia, and air-leak from the lung

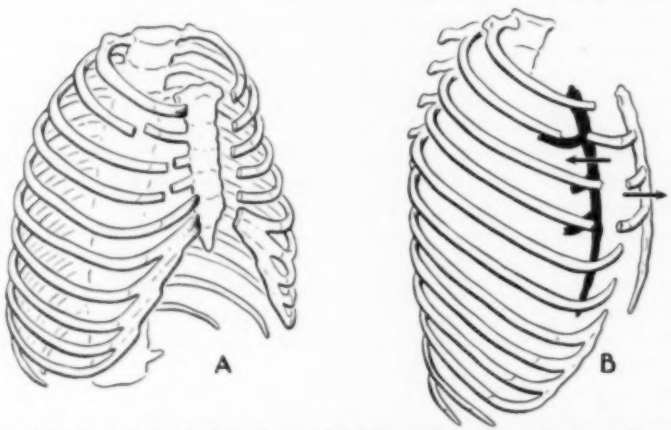

FIGURE 7: *Paradoxical Motion of Flail Sternum.* Sketch **A** shows types of rib fractures and chondral separations which result in paradoxical motion of sternum. — **B** shows the type of motion which results, the sternum sucking in with inspiration and bulging forward with expiration. Strapping cannot stop the inward paradoxical motion on inhalation and hence is non-effective. Skeletal traction is effective.[7]

into the pleural cavity (Figure 12). If the pleura be obliterated, air leaks into the subcutaneous tissues. Hemorrhage into the contused muscles, free pleural cavity, and lung occurs from these injuries and seriously depletes blood volume.

The sternum may be ripped loose from its moorings either at the costochondral junction or by fracture of the anterior ends of the ribs bilaterally with or without fracture through the body of the sternum or at its juncture with the manubrium. When this occurs the whole front of the chest becomes flail, sucking way in on inspiration and bulging forward on expiration; again serious ventilatory embarrassment occurs (Figure 7).

These injuries all result in a degree of ventilatory insufficiency which is incompatible with life unless steps are taken to stabilize the chest wall and re-establish efficient ventilation. In addition, the pleural complications must be recognized and adequately treated and the blood loss, which may be quite extensive, replaced by transfusion. Coughing is a mechanical impossibility for these people as the entire explosive force of the cough is dissipated in the paradoxical motion of the chest wall which it produces. Thus, bronchial secretions cannot be removed by the patient, and, as traumatic wet lung is constantly present, these patients rapidly drown unless the tracheobronchial tree is repeatedly evacuated by suction.

Unilateral multiple rib fractures with the production of a limited area of flail-chest can be handled in young people with good respiratory reserve by firm strapping of the chest wall to stop all paradoxical motion (Figure 5). This strapping must be circumferential. It must be put on snugly enough that it compresses the fractured side into a position of deep expiration and stabilizes it there. Naturally, this type of strapping stops all costal respiration on both sides, but it can be tolerated by a young person with good diaphragmatic motion. If the injury is high, efficient strapping can be carried out by bringing the tape or bandage around the shoulder point on the good side and around the chest on the bad side and thus freeing the ribs on the good side.

If multiple rib fractures are extensive, even though unilateral, so that the entire chest wall on the involved side has lost its stability, one cannot stabilize it by strapping. Even though the injured side is compressed down against the mediastinum it is still flail and will move on respiration, allowing mediastinal shift which interferes seriously with the ventilatory exchange of the uninjured side. Bilateral crushing injuries of the chest with bilateral loss of stability obviously cannot be handled by strapping. One cannot ventilate bilaterally compressed lungs. For these reasons, chest-wall strapping is hazardous in these extensive in-

juries. It impairs what little normal respiratory motion may yet be possible without accomplishing any real benefit. It, also, if survived, results in serious deformity of the thoracic wall and permanent loss of pulmonary function of marked degree.

Consideration of the pressure relationships which occur in normal respiration and are responsible for the paradoxical motion of the chest wall that has lost its architectural rigidity provides the clue for the successful management of these serious injuries. Intra-abdominal pressure is positive, varying with the tone of the abdominal muscles, but usually in the normal individual ranging in the neighborhood of 6 to 12 centimeters of water, fluctuating with the respiratory phase. Intrathoracic pressure is negative, ranging from minus 4 to minus 12 centimeters of water at quiet respiration. It is this differential of some 10 to 20 centimeters of water pressure which is responsible for the domed contour of the diaphragms. Intrathoracic pressure can be elevated by forced expiration against the glottis to very high positive levels but always automatically with this comes an increase in intra-abdominal pressure, ranging above that in the thorax.

Paradoxical motion of the flail chest occurs because on inspiration the intrathoracic pressure falls below the atmospheric pressure. The chest wall, lacking bony support, is compressed by atmospheric pressure. As it sags in it destroys the intrathoracic negative pressure which the patient produced to suck new air into his lungs. Expiration, if it is slowly carried out, will not elevate the intrathoracic pressure above atmospheric pressure, but, if hyperpnea is present, expiration will result in intrathoracic pressure above atmospheric pressure, and the flail chest wall will be displaced outwards, thus interfering with the patient's ability to empty his alveoli of used air. In effect, this enormously increases the amount of dead air in the lungs.

An individual with an intact thorax and good vital capacity increases his alveolar ventilation as needed by increasing first the depth of respiration. Dead air space, represented by the capacity of the nose, mouth, pharynx, trachea, and bronchi, amounts to around 180 cubic centimeters. Increasing the tidal air from 350 cubic centimeters at rest to 1,000 cubic centimeters with moderate exertion greatly reduces the percentagewise importance of this dead air space. If, however, due to painful splinting of the chest wall, partial collapse of the lung by hemothorax or pneumothorax, or loss of stability of the chest wall by multiple rib fracture, a patient is unable to deepen his respiration and thus bring more alveoli and vascular bed into the business of absorbing oxygen and eliminating carbon dioxide, he has only the recourse of increasing the rate of respiration. This is not efficient. Shallow

respiration provides poor exchange due to the high percentage of the air motion taking place in the dead air space. Increasing the rate results in little more alveolar ventilation under these circumstances. It largely accomplishes the exchange of more dead air. If the dead air space be greatly increased by paradoxical motion, it further magnifies this difficulty.

It is obvious that to ventilate more alveoli paradoxical motion must be stopped. This can be accomplished only by stabilizing the chest wall. If fractures of the sternum or bilateral parasternal rib fractures or costochondral separations have occurred with the production of anterior thoracic instability and a paradoxically moving sternum, traction tongs may be applied to the sternum and through these four or five pounds of traction applied to the sternum (Figure 8). This gives immediate relief, allowing effective exchange and good coughing. It solves the whole problem in quite a simple and dramatic way.[7]

Extensive loss of stability of the lateral chest wall cannot be dealt with by traction, but consideration of the pressure relationships of respiration mentioned above points the way. All that is necessary is to move the cycle of intrathoracic pressure changes responsible for ventilation above atmospheric level. Very adequate

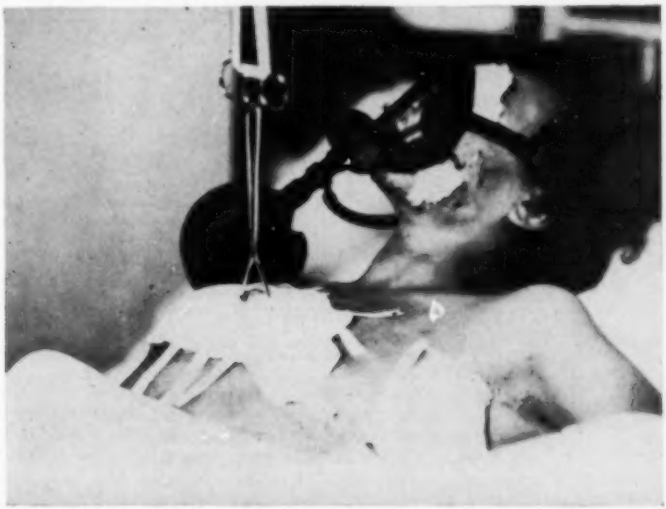

FIGURE 8: Photograph of patient in Minneapolis General Hospital with crushing injury of chest resulting in flail sternum. Traction tongs in place stabilizing this sternum by four pounds pull over pulley on Balkin overhead frame. (Photo courtesy T. J. Kinsella, M.D.).

exchange can be maintained on a 4 centimeter of water pressure differential between inspiration and expiration. All that must be done then is to provide an intratracheal pressure which never falls below atmospheric pressure on inspiration and which will rise 4 centimeters of water above atmospheric pressure on expiration (Figure 9). This can be done in several ways. A cuffed intratracheal tube passed through the nose or the mouth and attached to a source of oxygen arranged to deliver these pressures will do the trick. A tight-fitting face mask of the positive-pressure type, such as a meter positive-pressure mask will, likewise, do the trick and will stave off disaster until more tolerable and permanent arrangements can be made.

We have found the best solution to be a tracheotomy with the insertion of a specially modified tracheotomy tube. A small tracheal wound is made which fits the tube snugly. Neither a tightly fitting face mask nor an intratracheal tube can be tolerated for long periods of time for obvious reasons but a tracheotomy tube is well tolerated, and with slight modification can readily be attached to a properly arranged oxygen source. It functions not

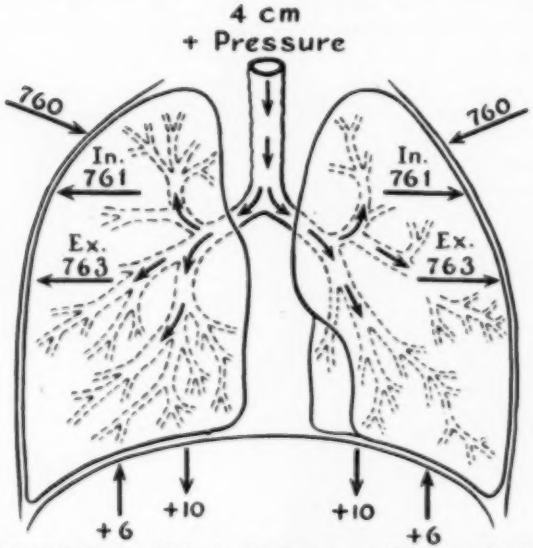

FIGURE 9: *Mechanics of Intratracheal Pressure.* Diagram showing effect of increasing intratracheal pressure 4 cm. of water above atmospheric (3 mm. of mercury). If expiration is against this positive pressure, intrathoracic pressure on expiration will be 763 (ex.), and inspiration will be somewhat less than this (in. 761) but still above atmospheric pressure. Since intrathoracic pressures are now always above atmospheric flail chest wall will be stabilized.

only as an airway but as an easily accessible port through which tracheobronchial aspiration can be carried out. The tracheotomy also has the additional advantage that it reduces the ventilatory dead space as it short-circuits the mouth and pharynx and upper trachea. Figure 10 shows such a modified tracheotomy tube and the adaptor used with it, and the legend below describes the parts and their function.

Proper equipment for the administration of oxygen through such a tracheotomy tube is not commercially available, but it can be readily made up in any scientific apparatus shop, utilizing largely the components standard for most gas anesthesia machines. The essential features are well illustrated in Figure 11. The oxygen is delivered from the usual cylinder through a reduction valve to a humidifying jar. From the humidifying jar it flows into a

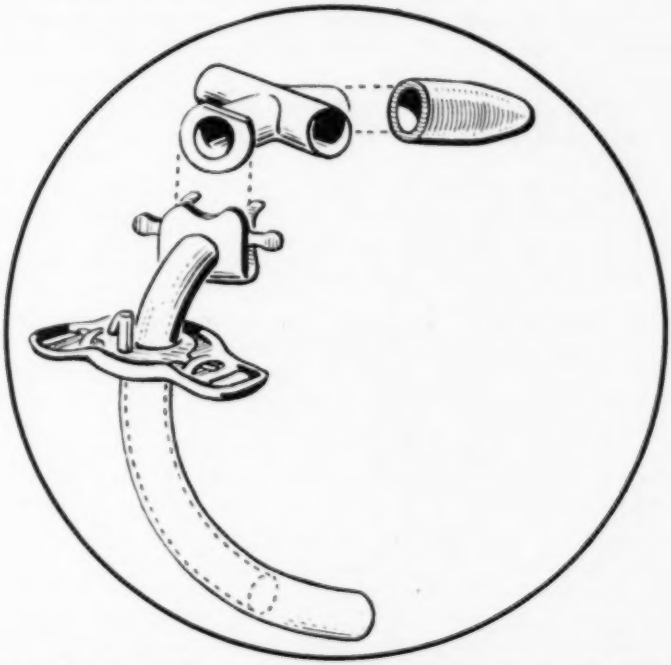

FIGURE 10: Ordinary No. 6 tracheotomy tube modified by soldering clip on inner tube to accept T adaptor. T adaptor made up of stainless metal tubing of same diameter as inner cannula of tracheotomy tube. Suction opening closed by rubber top of eye dropper. When inner cannula of tracheotomy tube is in place locking lever of tracheotomy tube secures both inner cannula and T adaptor in place. T adaptor should be made up with suction arm angled forward to avoid bumping against patient's chin.

large rubber collecting bag. This bag should be of thin rubber, easily distensible, with great elasticity. The ordinary anesthetic-machine bag will do, but it is small and too thick and rigid for efficient operation. The type of breathing bag provided with the positive-pressure meter mask is much better. It should be large enough that ordinary ventilatory exchange does not appreciably affect its volume (10 liters). From the bag the gas flows through a one-way valve into large corrugated anesthesia-machine tubing. The one-way valve should be made up in a Lucite block so that its function can always be assured by direct inspection. The corrugated tubing must be long enough to comfortably reach from the machine placed by the patient's bed to the tracheotomy tube. Here it should be attached by the shortest possible tubing of reduced size to fit the adaptor in order not to add undue resistance to the flow of gases. A similar tube should lead away from the tracheotomy adaptor and back to the oxygen administration equipment, where its end is placed under 4 centimeters of water.

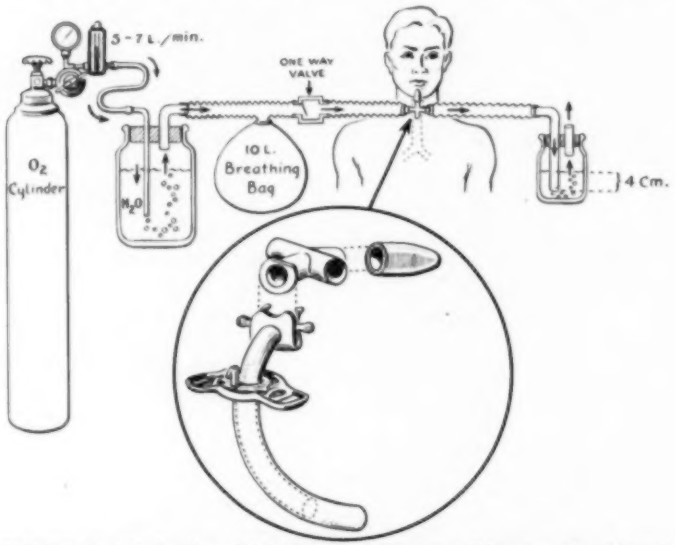

FIGURE 11: *Mechanics of Intratracheal Pressure.* Diagram of equipment used to deliver positive-pressure oxygen intratracheally. Oxygen is delivered from usual cylinder through reducing valve and flow meter to humidifying jar. Then flow is into large breathing bag and on through a one-way valve to tracheotomy tube. Exhaust from tracheotomy tube is immersed under 1 to 4 cm. of water, producing positive pressure in system of this magnitude. Oxygen flow must be adequate to compensate for loss by leakage about tracheotomy tube, etc., and still provide this pressure. Details of modified tracheotomy tube shown in inset given in Figure 10. (*Note:* Bag should be large and of good elastic recoil).

Obviously, there will be some leaking of oxygen out of the trachea, back around the tracheotomy tube, and out through the tracheotomy wound. There will, likewise, be some leakage between the adaptor and the tracheotomy tube. This can easily be compensated for by adapting the flow of oxygen to maintain the pressure in the system at the desired level despite the leakage. Usually 5 to 7 liters of oxygen per minute will accomplish this. When the machine is in operation, oxygen will bubble through the water on expiration against a head of pressure determined by the depth of the submersion of the discharge tube. On inspiration the bubbling may cease or almost so, but the water should not rise above its level in the lumen of the submerged tube. This would indicate that inspiration is occurring at pressures lower than atmospheric pressure. Under these circumstances paradoxical motion of the chest wall will again develop.

Positive-pressure oxygen will stabilize the flail chest wall in a position of moderate expiration. Since the intra-abdominal pressure is automatically controlled by the tone of the abdominal musculature, it will remain well above the intrathoracic pressure, and diaphragmatic respiration will be unaffected. The positive intratracheal pressure fully expands both lungs and provides a deep ventilatory excursion with good tidal air. The one-way valve between the collection bag and the tracheotomy tube prevents to-and-fro motion in the system and thus eliminates any dead air space factor in the apparatus, and carbon dioxide elimination is automatically accomplished.

This special tracheotomy tube and oxygen administration machine were first developed by Kottke, Kubicek, et al.,[5] of the Department of Physical Medicine of the Medical School of the University of Minnesota for the administration of intratracheal oxygen to patients with bulbar poliomyelitis. Their success with it has been brilliant, and in their hands this equipment has frequently replaced the use of the Drinker respirator in the handling of these patients.*

Figure 12 is made from the initial roentgenogram of a severe bilateral crushing injury of the chest. This is a man of 54 years who, after correction of his pneumothorax and clearing of his airway by repeated tracheobronchial aspiration, was unconscious from hypercarbia and with anoxic bradycardia and a rapidly advancing pulmonary edema despite 100 per cent oxygen administered by positive-pressure meter mask. Three hours after

*These authors did not describe this equipment for positive-pressure oxygen administration. Its application to this use has been by us in crushing injuries of the chest and other types of acute pulmonary edema.

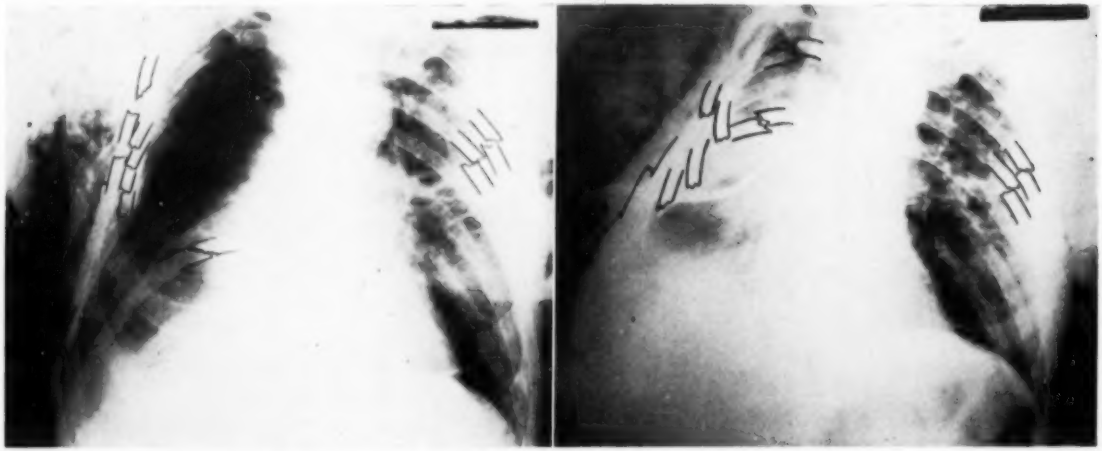

FIGURE 12 FIGURE 13

Figure 12: Admission roentgenogram of a 54-year old man admitted to Northwestern Hospital, Minneapolis, one hour after he sustained a crushing injury of the chest. Chest flail bilaterally with multiple bilateral rib fractures, only a few of which have been outlined by the artist to show the levels at which many occurred. Right pneumothorax and extensive subcutaneous emphysema. Patient anoxic, delirious, and in deep shock — *Figure 13:* Roentgenogram one hour later with suction catheter in right pleural space controlling pneumothorax, but right lung opacified by edema and hemorrhage and pulmonary edema advancing on left side. Patient still anoxic and in shock despite adequate blood replacement, tracheobronchial aspiration, and 100 per cent oxygen by mask. Chest still bilaterally flail. (See Figures 14 and 15).

tracheotomy and attachment to this machine he was conscious, rational, with a pulse below 100 and a respiratory rate in the twenties (Figures 14 and 15).

The management of pleural complications deserves some mention. Traumatic pneumothorax is best treated by immediate performance of a trochar thoracotomy and the insertion of a suction catheter. This is a simple procedure and may be done at the bedside under local anesthesia (Figure 13). The catheter should be firmly attached to the chest wall by some suitable means and attached to an underwater seal or promptly connected to a suction apparatus which will maintain a continuous negative pressure in the neighborhood of 16 to 20 centimeters of water. If air alone is collecting in the pleural space, a catheter placed anteriorly in one of the upper interspaces will evacuate the air and allow re-expansion of the lung. Sufficiently rapid suction must be applied to stay ahead of the air-leak and create a negative intrapleural pressure around 16 to 20 centimeters of water. As soon as the lung expands to the chest wall the air-leak will immediately seal off as it comes into contact with the parietal pleura. This is the only method which will safely control tenesion pneumothorax, and if tension has not yet developed at the time of the instillation of the catheter it will be completely avoided and additional pulmonary tissue will immediately become available for respiratory function.

If fluid and air are both present, it is sometimes necessary to use two catheters, placing one posterolaterally and feeding the tip into the paravertebral gutter next to the diaphragm and the other anteriorly as above described. The posterior catheter will remove the fluid and the anterior one the air. A well aspirated hemothorax is one that will not have to be decorticated. Every effort should be made to remove serum and blood as completely as possible and as quickly as possible from the pleural space, for the longer they remain the more fibrin will be laid down over the pleural surfaces, and this, in turn, will be converted to scar tissue which seriously cripples ventilatory motion and leads to respiratory crippling.

The recovery of pulmonary function after thoracic injury occurs in two phases. The initial phase covering the time from the injury to the re-establishment of sufficient respiratory capacity to be compatible with life is a struggle which must be won in the first few hours after injury. Several days to a week of continuous effort may be necessary to secure this victory. There then follows a prolonged program to regain as much ventilatory motion of thoracic cage and diaphragms as possible.

If hemothorax has occurred and clotted before it could be suc-

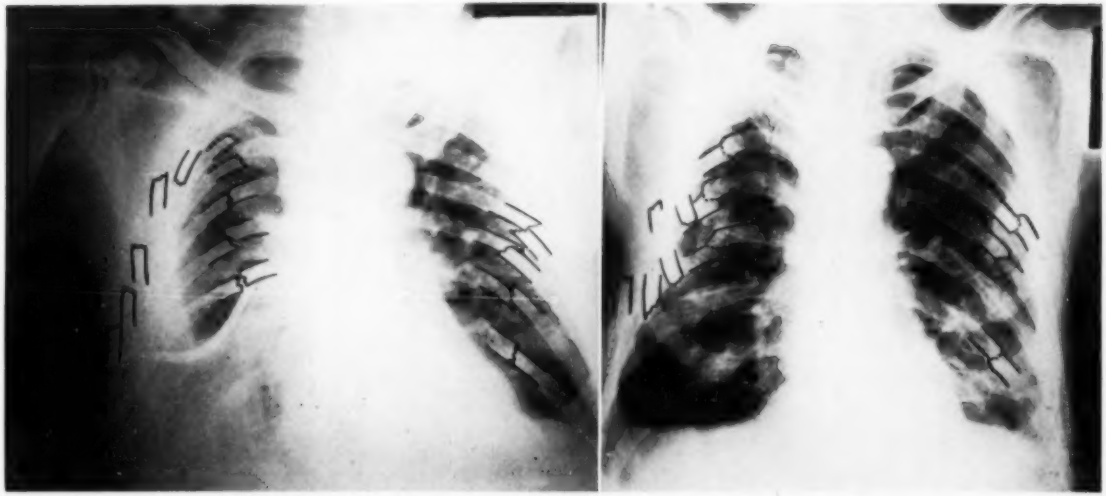

FIGURE 14

FIGURE 15

Figure 14: Roentgenogram showing tracheotomy tube in place with considerable clearing of right lung, three hours after establishment of positive-pressure intratracheal oxygen. Patient now rational, with physiological pulse, blood pressure, and respiration. Chest stable; no paradoxical motion. — *Figure 15:* Roentgenogram of same patient as shown in Figures 12, 13 and 14, four months later. Aeration of both lungs good but respiration painful on right side. Fluoroscopy at this time showed false motion at posterior fracture sites on left. Artist has sketched in three of these showing offset. As firm union occurred at these fractures pain subsided and function improved. Final vital capacity 70 per cent of normal for age and habitus.

cessfully aspirated, decortication of the lung should be undertaken as soon as the patient's general condition permits, for otherwise the function of this lung will be permanently lost and the hazard of chronic empyema is great. Decortication meticulously carried out with removal of both the parietal and visceral peel and with care to remove the mass of scar tissue which forms in the costophrenic sulcus results in excellent return of pulmonary function even though the operation must be delayed weeks to months by other complications.[6] Figure 16 shows the roentgenogram of a traumatic hemothorax one month old. Figure 17 is a roentgenogram of this chest 20 days after decortication. Figure 18 shows the differential pulmonary study as revealed by differential bronchospirometry. Ventilation and oxygen uptake are excellent on both sides.

Extensive multiple fractures of the ribs accompanied by disruption and laceration of the intercostal musculature heal with considerable fixation of the thoracic wall. These people have a painful chest for weeks with resultant immobilization. Atrophy of the intercostal musculature follows, and occasionally bony bridging between the ribs occurs. Breathing exercises started early by a physiotherapist trained in the art of respiratory exercises will do much to avoid this crippling fixation of the thoracic cage. Many of these people forget how to use their intercostal musculature

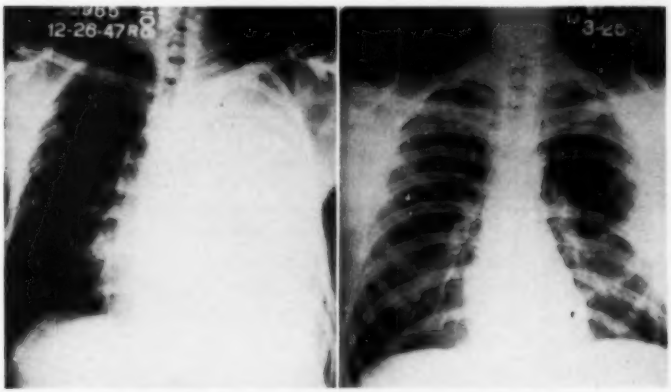

FIGURE 16

FIGURE 17

Figure 16: Left traumatic hemothorax one month old. Clotting has occurred, and aspiration is impossible. Patient febrile and losing weight (20 pounds since injury).—*Figure 17:* Roentgenogram of same chest 21 days after decortication. Both parietal and visceral peel of parapleural scar tissue removed at surgery. Patient now receiving intensive respiratory exercises. (See Figure 18).

during the period of painful immobilization and must be retrained.

Persistent thoracic wall pain deserves careful consideration by the thoracic surgeon as it may signify non-union of rib fragments with pain on motion occurring at these old fracture sites (Figure 15). False motion at fracture sites of the ribs can be discovered on fluoroscopy and their role in the production of the painful chest established by novocain block. Chest-binder immobilization may allow these fragments to heal and result in an earlier toleration by the patient of vigorous progressive thoracic exercises than is otherwise possible. However, if after six weeks to two months of immobilization the painful false motion still persists it is better to expose the fracture site and freshen up the ends so that union may occur.

Persistently painful costochondral articulations will immobilize a chest and are somewhat more difficult to spot. They cannot be demonstrated in the roentgenogram or fluoroscopy, but careful palpation will localize the tenderness and frequently a click may be produced by pressure on the articulation. Occasionally the patient will describe the clicking and relate it to the pain experienced. If these have not united by six months after injury, they should be excised subperichondrially so that firm bony regeneration will occur with good union. This stops the pain and allows the return of good motion of the chest wall.

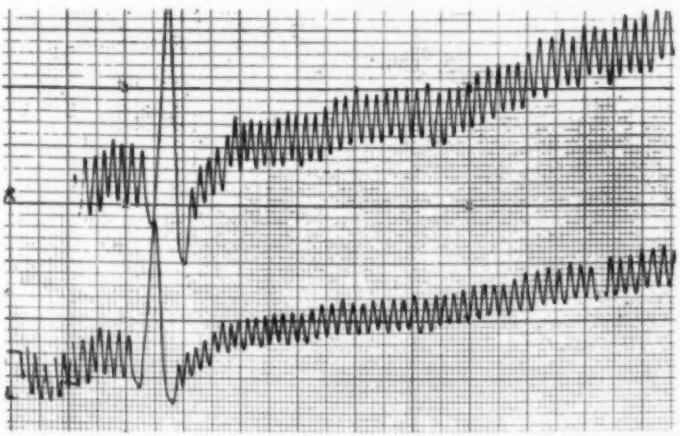

FIGURE 18: Differential bronchospirometric tracings of same patient shown in Figures 16 and 17, about three months after decortication. Lower tracing is injured side. Tidal air, minute volume, and vital capacity still not quite as good as uninjured side but oxygen uptake about equal. Further improvement will occur.

SUMMARY

The recovery of pulmonary function following crushing injury of the chest occurs in two phases. The early period after injury, during which time the battle for survival must be won, is one of seriously disturbed ventilation and vascularization of alveolar spaces. The second phase is characterized by residual disturbances in the thoracic musculoskeletal system and the pleural spaces. These must be corrected if efficient respiration is to be regained.

Minor crushing injuries with little or no paradoxical motion of the chest wall require strapping to stabilize the chest wall and relieve pain, tracheobronchial aspiration to maintain adequate airway, and little else. Pulmonary edema will occur in some degree in even these injuries and requires oxygen. If pulmonary edema is severe, the oxygen should be administered under positive pressure.

Severe crushing injuries involving one or both sides require tracheotomy with repeated catheter evacuation of tracheobronchial secretions and positive-pressure oxygen for a sufficient period to allow stabilization of the chest wall. Blood loss may be extensive and will require volumetric replacement. Pleural complications of hemothorax and pneumothorax require immediate catheter thoracotomy and suction drainage. Spreading and bothersome subcutaneous emphysema is promptly controlled by tracheotomy.

Decortication of all fibrinothoraces without undue delay will salvage pulmonary function in the second phase, particularly if every effort is made to redevelop the motion of the crippled side by early and persistent muscle training and respiratory exercises.[6] Non-union of ribs and costochondral cartilages require resection for cure. These non-unions are painful and must be eliminated if good function is to redevelop.

RESUMEN

La recuperación de la función pulmonar después de las lesiones por compresión ocurre en dos fases. El periodo temprano después de la lesión durante el cual la batalla por la sobrevida debe ganarse, es en el que ocurren serios trastornos de la ventilación y de la vascularización de los espacios alveolares. La segunda fase está caracterizada por trastornos residuales en el sistema musculoesquelético torácico y en los espacios pleurales. Estos deben ser corregidos si se trata de recuperar la respiración eficiente.

Las lesiones por compresión, menores, con movimiento paradójico pequeño o nulo del torax requieren fijación de la pared por tela adhesiva y calmantes del dolor, aspiración traqueobronquial para mantener la permeabilidad de las vías aéreas y poco mas. El edema pulmonar puede aparecer en cierto grado aun en esas

lesiones y requiere el oxigeno. Si el edema pulmonar es severo el oxigeno debe administrarse bajo presión positiva. La lesion por compresión, severas, que comprometen uno o los dos lados requieren traqueotomía con repetida evacuación de las secreciones por el catéter y oxégeno a presión por un tiempo suficientemente largo para permitir la fijación de la pared del torax. La pérdida de sangre puede ser grande y requerir reemplazarla volumétricamente. Las complicaciones pleurales de hemotorax y neumotorax requieren inmediata toracotomía con cateter y canalización-aspiración. El enfisema invasor subcutáneo se domina prontamente por la traqueotomía.

La decorticación de todos los fibrotorax sin dilación indebida logrará rescatar la función pulmonar en la segunda fase particularmente si se hace todo esfuerzo para re-desarrollar el movimiento del lado afectado por medio de entrenamiento muscular y ejercicios respiratorios tempranamente. La falta de union de las costillas y de las articulaciones condrocostales requerirá resecciones subcondrales para la curación. Esta falta de unión es dolorosa y debe ser eliminada si se quiere obtener la recuperación funcional buena.

RESUME

La restitution de la valeur fonctionnelle du poumon après écrasement thoracique se fait en deux phases. La période qui suit immédiatement l'accident, au cours de laquelle il faut gagner la bataille dont l'enjeu est la vie, est accompagnée de troubles graves de la ventilation et de la vascularisation des espaces alvéolaires. La deuxième phase est caractérisée par l'existence de troubles résiduels des plèvres et du système musculaire et osseux du thorax. Lorsque la respiration efficace réapparait, ces troubles sont réparés.

Les petits écrasements avec mobilité thoracique légère et non paradoxale demandent un bandage pour immobiliser la paroi thoracique et supprimer la douleur, et une aspiration trachéo-bronchique pour amener la perméabilité des conduits. Même dans ces traumatismes peu importants, on peut voir apparaitre un oedème pulmonaire qui nécessite l'oxygénothérapie. Si l'oedème pulmonaire est grave, l'oxygène devra être administré en pression positive.

Les écrasements thoraciques graves atteignant soit l'un des côtés, soit les deux côtés, exigent la trachéotomie avec évacuations répétées des secrétions trachéo-bronchiques à la sonde. Il faut y ajouter l'oxygène en pression positive. Ce traitement doit être fait pendant une période suffisamment prolongée pour permettre la réconstitution de la paroi thoracique. La perte de sang peut être importante, et on doit en restituer une quantité égale. Les complications pleurales (hémothorax et pneumothorax) exigent la mise

en place d'une sonde et l'aspiration. L'emphysème sous-cutané est rapidement combattu par trachéotomie.

Il ne faut pas trop tarder à pratiquer la décortication de tous les éléments fibrineux dans la deuxième phase. Ainsi pours être sauvegardée la fonction pulmonaire, si on multiplie les efforts pour restituer la mobilité du côté atteint grâce à des exercices musculaires et respiratoires précoces et longtemps continués. L'absence de réparation des côtes ou des articulations chondro-costales demande à être traitée par résection sous-périostée. Il faut éviter que les fragments osseux restent désunis, car ils sont elas douloureux, et s'opposent au retour d'une bonne fonction pulmonaire.

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Discussion

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Recently, Dr. O. L. Bettag and I gathered together material for the Civil Defense Commission of Chicago on chest injuries and we found that to properly treat these wounds, one had to be acutely aware of how to correct the deranged cardio-respiratory physiology. With this point in mind, I should like to emphasize several of the points Dr. Jensen raised, in perhaps a somewhat different fashion.

World War II brought forcibly to our attention, the necessity for better care for chest wounds. The extensive experience of the 2nd Auxiliary Surgical Group permitted Burford, Burbank, Brewer, Samson, Shafts, Betts, Lees and others to publish observations

which led to better understanding of traumatic wet lung, clotted hemothorax, and thoracoabdominal wounds. We saw repeatedly how the incidence of wet lung went up in the winter months when many of the troops had bronchitis of varying severity. Also, this entity occurred even when little or no sign of external injury was present.

Every patient with a chest injury will present a picture of altered intrathoracic physiology varying in intensity, with the severity of the wound. Thus, we may safely say that shock, pain, dyspnea, and cyanosis will be present. Treatment must be directed toward the eradication of these signs and symptoms.

Pain may be responsible for all the other signs, as intimated by Dr. Jensen. In my experience, chest pain is best relieved by intercostal nerve block proximal to the site of injury, in most instances best performed para-vertebrally. I do not think it need necessarily be performed by an expert, for anyone who can give pneumothorax can easily learn the anatomical relationships needed to perform an effective nerve block. It is distressing to see a patient in shock, with severe pain, cyanosis and moist bubbling respirations, unable to cough because of the pain. After an adequate intercostal nerve block it is surprising to see the transformation as effective coughs eliminate moisture from the tracheobronchial tree and better oxygenation of the blood occurs. If this is ineffective, tracheal catheter aspirations as advocated by Haight is used. Bronchoscopy is the last resort but must not be overlooked. One must keep in mind that bronchoscopy will excite a bronchorrhea of itself. If the patient is comatose an endotracheal tube can be inserted and alternately oxygen can be administered under pressure or the bronchial aspiration carried out (frequently through the same catheter). If the patient does not respond after 24 to 48 hours, then tracheotomy is indicated. The B.L.B. mask is useful for positive pressure oxygen but very ill patients or those restless from anoxia will not tolerate it and therefore, I am intrigued by the method Dr. Jensen described.

Sedatives: morphine in particular should be used with great caution. Not uncommonly, we saw wounded boys given morphine on the battlefield for pain, who being in shock, could not absorb it quickly. During transportation pain was again experienced or being restless from anoxia and more morphine was given. When the shock is corrected the depot of morphine, so to speak, is absorbed rapidly and the result is a deeply narcotized patient; a dangerous state for the patient with an injured thorax.

One must determine whether the shock is due to blood loss and then only blood transfusions are needed to correct it. Hematocrit determinations are easily and quickly performed and best indicate

the need for blood. It is best to avoid using saline or dextrose infusions in such instances.

I cannot subscribe to the use of a wide circumferential adhesive strapping in chest injuries. In women who are costal breathers in the main, the decreased pulmonary ventilation caused by the circumferential binding might be more than the diaphragm can compensate for and so hypoxia will be increased. Intercostal nerve block alone will adequately control pain. If strapping is desired then a single band of three inch tape completely around the chest at the costal margin in expiration will suffice. Anatomical physics explains why, if the lower ribs are immobilized, the upper chest can expand but slightly on inspiration. If paradoxical motion of the chest wall is not prevented by this means, it may become necessary to use mechanics waste and elastoplast dressing, a sand-bag, or in the case of the flail chest, towel clips, screws, or a tenaculum to the sternum and traction with weights must be applied.

Thoracentesis of blood and air or both must be done promptly. The blood aspirated should not be replaced by air. No one can tell which patient will have clotted hemothorax. Some clotted within hours after injury and some could be aspirated days later. All liquid and air should be aspirated promptly to permit re-expansion of the lung. If clotting does occur decortication is best performed in about six weeks. The peel is easily removed at this time. Delay after six weeks leads to organization and vascularization and decortication then is dangerous, since more bleeding is encountered and the lung is torn thus producing many bronchial fistulae which could conceivably lead to empyema and again a so-called captive lung results. Enzymatic decortication if used early enough, may prevent some operations.

Sucking wounds should be closed on sight with a vaseline gauze dressing until proper debridement and closure can be effected. Not all hemopneumothoraces require immediate catheter drainage. The use of the "educated" needle may permit aspiration of blood and air and manometric readings may indicate that the fistulae have become sealed. If pressure or tension pneumothorax recurs, water-seal drainage is indicated. I prefer a flanged catheter of the Pezzar or Malecot type to the trocar and ordinary urethral catheter, since placement is more accurate with the former and injury to lung, which may be close to the parietal pleura by the trocar, can be avoided. If the lung does not re-expand within a reasonable period of time, suction is applied as Dr. Jensen indicated.

One additional factor that must be recognized is that in any crushing injury a lower nephron nephrosis may occur. Prompt and early alkalinization with one-sixth molar lactate solution or sodium

bicarbonate solution may aid in preventing mortalities from this cause.

The use of bronchospirometry in this type of injury is important and Dr. Jensen and Dr. Wood and Dr. Peterson are to be commended for their contribution to cardio-respiratory physiology. Without a doubt, prompt recognition and adequate early treatment of chest injuries will result in better recovery of pulmonary function.

Bronchogenic Carcinoma and Chromates*

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Although in Germany the medical profession and industrialists have recognized the increased incidence of primary lung cancer in chromate workers ever since Pfeil reported two cases in 1935, in the United States with the exception of a comprehensive article bu Hueper in 1942 discussing the toxic effects and cancerigenic properties of chromates, this very serious public health hazard was allowed to remain dormant until Machle in 1948, and Mancuso in 1949, reported the disproportionate increase of primary lung cancer in the chromate industry.

The author in a limited search in a chromate plant of 400 employees with an annual turnover of about 40 to 50 per cent, discovered in a 10 month period between May 1947, and March 1948, seven cases of primary lung cancer. In addition, several other cases presented suspicious symptoms—but they could not be followed.

Briefly, the known clinically toxic effects of chromate exposure are as follows: dermatitis and ulceration; conjunctivities; varying degrees of inflammation of the respiratory tract ranging from rhinitis, sinusitis, and bronchitis—occasionally asthmatic, to ulceration of the mucous membrane and in severe cases perforation of the cartilaginous portion of the nasal septum; hyperplasia of the bronchial epithelium; deposit of chrome pigment along the lymph channels of the lung and mediastinum; and as the case histories reported below will corroborate, neoplastic changes of the bronchial epithelium.

Case Histories

Case 1 (J.G.): Age 62 years; Negro; exposure for nine years; first seen by the author in May 1947; complaining of cough, expectoration, shortness of breath, hoarseness, marked weakness, occasional wheezing and a loss of 17 pounds in weight the previous six months. His cough dated to January 1946, and an x-ray film on January 24, 1946 (Figure 1a), demonstrated a nodular mass arising from the right hilus. Bronchoscopic examination in April 1946, showed torsion and deviation of trachea to the right. He failed to improve and an x-ray film on May 18, 1947 (Figure 1b), showed an increase in size of previously described mass. He was hospitalized in October 1947, and on bronchoscopic examination a mass was found protruding from the orifice of the right upper lobe bronchus,

*Presented at the First International Congress on Diseases of the Chest, Forlanini Institute, Rome, Italy, September 19, 1950.

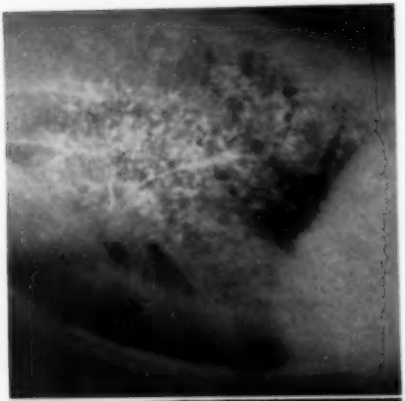

FIGURE 2c

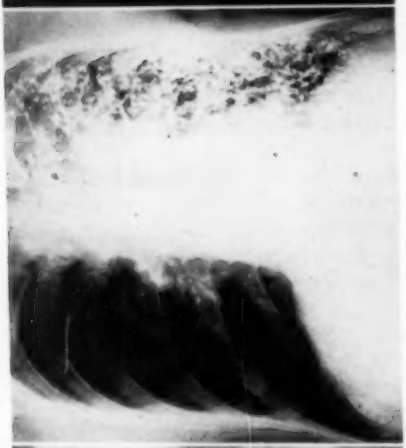

FIGURE 2b

FIGURE 2a

that on histological examination proved to be an oat-cell carcinoma, bronchial in origin. On October 16 exploratory thoracotomy revealed an inoperable carcinoma of the right upper lobe. He died on November 11, 1947.

Case 2 (J.G.): Age 45 years; white; exposure for 20 years; first seen by the author in May 1947; complaining of severe distressing cough with expectoration occasionally blood streaked; wheezing; pains in the chest; weakness; difficulty in swallowing; and a loss of 12 pounds in weight during the previous nine months. Clinically, the trachea was deviated to the left and breath sounds were diminished over left chest anteriorly above the fourth rib. A chest x-ray film on May 28, 1947 (Figure 2a), showed enlargement of the left hilar shadow. Repeated bronchoscopic examination revealed varying degrees of congestion and thickening of the bronchial epithelium throughout both lungs, more pronounced on the left side; however, both sputum and bronchial lavage studies failed to reveal cancer cells. A bronchogram taken on December 9, 1947 (Figures 2b and 2c), revealed definite pooling of lipiodol at the level of the left upper lobe bronchus. He was hospitalized and an exploratory thoracotomy performed December 12, 1947 revealed an inoperable lemon-sized tumor originating from the left upper lobe bronchus, that had metastasized to the mediastinum, pushing the oesaphagus to the left, invading the arch of the aorta and incorporating the left recurrent laryngeal nerve. Biopsy of a bronchial lymph node revealed a transitional-cell carcinoma, bronchial in origin. Five months later, because of inability to swallow, a therapeutic gastrotomy was done and he died October 29, 1948.

Case 3 (H.P.): Age 50 years; exposure for 25 years; first seen by the author on July 15, 1947; complaining of having had "grippe" and extreme weakness for the previous two weeks, and an incessant cough of at least six months duration. Chest x-ray film taken in April 1947 (Figure 3a), was interpreted as normal. However, he failed to recover from "grippe"; cough became worse complicated by expectoration of increasing amounts

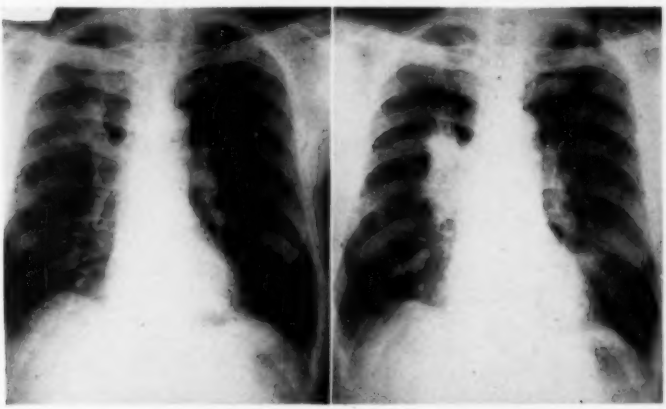

FIGURE 1a FIGURE 1b

FIGURE 4

FIGURE 3b

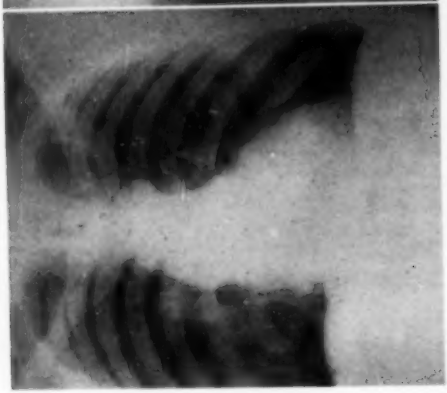

FIGURE 3a

of bloody sputum; also wheezing and extreme weakness became prominent symptoms. The bronchial wheeze was heard best over the right chest anteriorly. Chest x-ray film taken July 22, 1947 (Figure 3b), revealed infiltration of the right upper lobe. On August 15, 1947 bronchoscopy demonstrated a bleeding mass protruding from the orifice of the right upper lobe bronchus. He was hospitalized and on September 3 an exploratory thoracotomy uncovered a large marble-like tumor of the right upper lobe invading the parietal pleura. Histologically, this proved to be an undifferentiated-cell carcinoma. He died on November 5, 1947.

Case 4 (J.B.): Age 59 years; exposure for nine years; first seen by the author in November 1947; complaining of cough relatively unproductive, of at least two years duration and more recently of weakness and indefinite weight loss. On November 13, 1947 a chest x-ray film suggested an increased hilar shadow on the right side. On December 15, 1947 he was suddenly striken ill, hospitalized, and diagnosed provisionally as "cardiorenal disease" but within 18 hours he was dead. Postmortem was conducted by the medical examiner in conjunction with the author, and there was found a (1) degenerating primary carcinoma of the middle lobe bronchus; (2) chronic bronchitis and bronchial thickening; (3) diffuse lymphadenopathy of the chest; (4) obliterative pleuritis on the left; and (5) enormous deposits of pigment throughout the lymph channels of the lung and mediastinal lymph nodes. Histologically the carcinoma proved to be transitional-cell in type.

Case 5 (J.S.): Age 50 years; Negro; exposure for 20 years; first seen by the author in May 1947, complaining of cough and expectoration of thick greenish sputum, extreme weakness and loss of 35 pounds in weight during the previous six months. His cough had been an annoying symptom for at least five previous years. In December 1946, he had a severe illness diagnosed as pneumonia. However, he failed to recover, and at first he was thought to have unresolved pneumonia. Six months later, in May 1947, examination by the author revealed an extremely emaciated pa-

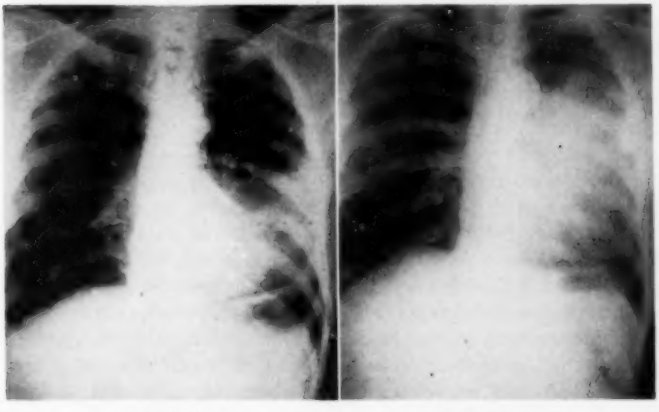

FIGURE 5a FIGURE 5b

tient; a sentinel node was readily palpable on the left side. X-ray films of chest on February 24, 1947 and May 21, 1947 (Figures 5a and 5b), revealed a homogenous shadow involving the entire left lower lobe. On the last film, the density coalesced uniformly with the cardiac shadow. Unfortunately, biopsy of the nodes was not completed. He died on August 24, 1947. Postmortem examination could not be obtained. Clinically and radiologically, this patient followed a course of bronchogenic carcinoma with atelectasis and pneumonitis, of the lower lobe of the left lung.

Case 6 (Z.R.): Age 57 years; white; exposure for 15 years; apparently in good health; stricken with pulmonary symptoms diagnosed at first as pneumonia with x-ray film evidence of apparent consolidation of the entire right upper lobe. However, he failed to recover and after a relatively afebrile period of eight weeks, expired on November 8, 1947. Postmortem examination could not be obtained. Clinically and radiologically, this patient died of a right upper lobe bronchogenic carcinoma.

Case 7 (J.S.): Age 54 years; Negro; exposure for 15 years; was first seen in a university hospital on June 12, 1947, and the next day, following bronchoscopy, he died. Clinical and laboratory findings were recorded as follows: Carcinoma of the right lung, upper lobe, metastases to right supraclavicular node histologically found to be an undifferentiated-cell type of carcinoma.

Discussion

To understand properly the most likely modus operandi of cancerigenesis as may be applied to chromates, a brief mention of the chemistry of chrome and reference to laboratory research follows: Chromium is a heavy metal having an atomic weight of 52, and it is of the same family as Molybdenum, Tungsten and Uranium. Chromium is found in nature almost exclusively as ferrous chromite, $FeCr_2O_3$ or $Fe(CrO_2)_2$ and mined principally in South Africa. For usage in various industries the ore is processed in chromate plants into two main compounds: (1) the stable trivalent chromic, and, (2) the unstable hexavalent chromates. These latter compounds, the mono and dichromates, are powerful oxidizing agents and in the presence of organic matter the chromates, within a few hours, are converted into chromic compounds. There is reason to believe (Hueper) sodium dichromate exerts a quinogenic action on certain aromatic hydrocarbons and cyclic amines that may explain in part the chemical factor of cancerigenesis.

Other heavy metals have been shown to produce lung cancer. Of these, the occurrence of lung cancer in the Schneeberg Mine Workers is irrefutable. Hill and Fanning reported in a factory handling inorganic compounds of arsenic between 1910 and 1943 a cancer incidence of 29 per cent as compared with an incidence of 13 per cent in three comparable groups. In addition the present author (S.I.) had occasion to study histologic sections of lungs removed from patients dying from berrylium pneumonitis and

noted definite evidence of metaplasia and in isolated microscopic fields many cells of the bronchiolar epithelium displaying the cytological appearance of carcinoma. Recently, Abrahamson and associates in Ireland reported the development of a primary alveolar tumor of the mucous-secreting type in both lungs of a woman who 16 years previously had received 75 cc. injection of thorotrast for splenic enlargement. Also, workers in copper nickel refineries have an excessive liability to cancer of the nares and lung (Amor). Too, asbestosis seems to confer a similar liability as to lung cancer (Merewether).

However, other factors may play a role in cancerigenesis. The report of Winternitiz, Grove and Cramer, that during epidemics of influenza the infection had a definite tendency to produce diffuse pneumonic and bronchiolar types of lung cancer, proposes the possibility, since it is known in many humans the virus of influenza is found in their respiratory tracts without causing symptoms, perhaps in long standing exposure the virus may be activated.

Obviously from an analysis of the case histories reported by the author, one of the responsible factors in chromate workers is duration or extent of exposure in individuals having a susceptible or reactive respiratory tract. In the series of 47 primary lung cancers found from 1912 to 1943 by Gross and Kolsch in Germany, the range of duration from onset of exposure to clinical appearance of the disease was seven to 17 years; in Machle's series, the mean duration was 14.5 years; the author's series averaged 16 years. In Mancuso's series, the latent period—based on the clinical appearance of cancerigenic development following cessation of exposure to chromates— averaged at least five years. It must be borne in mind a most important factor is the concentration of chromate particles in the atmosphere. According to the United States Public Health Reports, the maximum concentration of chromate compatible with good health and prevention of nasal perforations has been found to be no greater than 1 mgm. per cubic foot of air. In the author's series, all cases were exposed to concentrations well in excess of the accepted values; all had nasal perforations.

SUMMARY

The author wishes to emphasize the following: During the 10 month period of investigation, all deaths occurring in this plant were due to carcinoma of the lung. Taking into consideration that an annual turnover of 40 to 50 per cent influences computation of the number of employees, I found the total number did not range more than 600. Since, of the series of seven cases, one died

beyond the annual period, the incidence of carcinoma was at least one in 600 employees. In the same state of two million population, the death rate from primary lung cancer averages 10 cases (men and women inclusive) per 100,000 annually. In comparable figures, the death rate in the plant would constitute 166 in 100,000 or an incidence at least 166 times greater than found in the rest of the population. This figure positively eliminates consideration of any mathematical or problematical error.

All in all, the evidence in the past and by the present author is much too emphatic to allow any view other than chromates are definitely cancerigenic: susceptible individuals, exposed to atmospheric concentrations of more than 1 mg. per cubic meter of air, for a duration of an average of seven years—perhaps less—are subject to develop bronchogenic carcinoma.

RESUMEN

Durante el periodo de 10 meses en que se llevó a cabo la investigación, todas las muertes en esta fábrica fueron originadas por carcinoma del pulmón. Tomando en cuenta que un movimiento de personal anual del 40 al 50 por ciento influye en el cómputo del número de empleados, puede apreciar que el número total no pasaba de 600. En vista de que, en la serie de siete casos, uno murió más allá del periodo anual, la incidencia de carcinoma fué por lo menos de un empleado entre 600. En el mismo estado, con una población de dos millones, el índice de muertes por cáncer primario del pulmón arroja un promedio anual de 10 casos (incluyendo hombres y mujeres) por cada 100,000. En cifras comparables, el índice de mortalidad en la fábrica sería de 166 en 100,000, o sea, una incidencia por lo menos 166 veces mayor que la que se ve en el resto de la población. Esta cifra elimina absolutamente toda consideración de algún error matemático o problemático.

En resumen, la evidencia que se ha presentado en el pasado y la del autor, es demasiado emfática para dar lugar a opinión alguna que no sea que los cromatos son definitivamente cancerígenos: los individuos susceptibles que quedan expuestos a concentraciones atmosféricas de más de 1 mg. por metro cúbico de aire durante un promedio de siete años—quizá menos—están propensos a desarrollar carcinoma bronquiogénico.

RESUME

Pendant une période de recherche de dix mois, tous les décès survenus dans une usine (usine de chromates) eurent comme cause le cancer du poumon. Prenant en considération que le renouvellement annuel de 40% des employés joue un rôle important sur l'effectif total à considérer, l'auteur estime que le nombre total

des ouvriers ne doit pas être tenu pour supérieur à six cents. Etant donné que dans la série des sept cas considérés, il y eut un mort par année d'observation, on peut admettre que la fréquence du cancer fut au moins de un pour 600 ouvriers. Dans le même pays comprenant une population de deux millions d'habitants, la moyenne du cancer primitif du poumon s'élève chaque année à 10 pour cent mille. Si no mettait en parallèle ces deux statistiques, on constate que dans l'usine considérée la moyenne de mortalité par cancer pulmonaire serait environ de 166 pour cent mille, c'est-à-dire 166 fois plus élevée que celle qui a été trouvée pour le reste de la population. Ces considérations éliminent d'une façon formelle toute erreur due au calcul ou au jeu du hasard.

Dans l'ensemble, il est évident pour l'auteur que les chromates sont cancérigènes. Les individus sensibles, lorsqu'ils sont exposés à une concentration de poussiéres de plus de 1 mmgr. par mètre cube d'air pendant un temps moyen de sept années, peut-être même moins, sont susceptibles de contracter un cancer bronchique.

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Fibrinous Pericarditis Secondary to Esophageal Ulceration*

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Most frequently, fibrinous pericarditis is associated with such illnesses as rheumatic fever, tuberculosis, sepsis, uremia and scarlet fever. More uncommonly, the entity of so-called idiopathic pericarditis is recognized when no primary etiology is present.[1,2] In addition, fibrinous pericarditis may occasionally result from infectious processes in contiguous structures, especially those of pleural and mediastinal location.

Fibrinous pericarditis, secondary to esophageal ulceration, however, is rare, and a review of the literature of the last 15 years fails to show any mention of it. It is for that reason that this case is considered of sufficient interest to be reported. Our patient presented in addition an extra-renal uremia, which was a puzzling point of clinical differential diagnosis.

Case Report: The patient was a 54 year old white male, who for one year prior to admission complained of dysphagia, which had caused him to subsist almost entirely on a liquid diet. Six to eight weeks before admission he began to complain of weakness and aching in the lower extremities, with several episodes of stumbling and falling. One week prior to admission he fell, fracturing his right fibula. This was accompanied by a transient episode of aphasia. Two days prior to admission he became increasingly weak, and was in shock when admitted on November 12, 1950.

At that time, the blood pressure was imperceptible, and the pulse weak and thready. Typical signs of shock were noted. There was a to-and-fro friction rub audible over the precordium and left sternal border. The patient was treated with the intravenous administration of whole blood, glucose and saline, totalling between 3,000 and 5,000 cc. of fluids daily, with the addition of Nor-Epinephrine. This was continued until November 16, 1950, when his blood pressure maintained itself without treatment. During the course of his entire hospital illness his rectal temperature fluctuated between 99 and 101 degrees Fahrenheit, and the urinary output was considered adequate.

The EKG showed non-specific T wave changes, suggestive of subacute pericardial disease.

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*From the Laboratory Service, Brooklyn Veterans Administration Hospital, Brooklyn 9, New York.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are a result of his own study and do not necessarily reflect any opinion or policy of the Veterans Administration.

On November 12, 1950 the WBC was 6,950, with a shift to the left, and a RBC of 4.1 million. The BUN level on November 12, 1950 was 140.0 mgm. per cent. It dropped steadily until on November 18, 1950, one day before death, it was 32.5 mgm. per cent. The CO_2 combining power was 27.7 Vol. per cent on November 12, 1950, but by November 17, 1950 had returned to 60 Vol. per cent.

The urine on three different occasions showed the specific gravity to vary between 1.014 and 1.020, with a consistently negative sugar and albumin reaction, and occasional WBC in the sediment. The Kahn test was negative.

His condition maintained a steady course for two and a half days, but on November 19, 1950 he again lapsed into shock, and died shortly thereafter.

Autopsy Findings: (Positive findings only).

Gross Findings: The heart weighed 500 Gms. The visceral and parietal pericardia were fused by moderately firm grey-pink shaggy adhesions, which could be severed without difficulty. There was no pericardial fluid. The remainder of the heart showed no significant gross changes.

The esophagus had a bright red to grey mottled mucosal surface. Six cm. above the gastro-esophageal junction was an oval ulcer, measuring 1.5 by 1.0 cm. in diameter, with its long axis parallel to the course of the

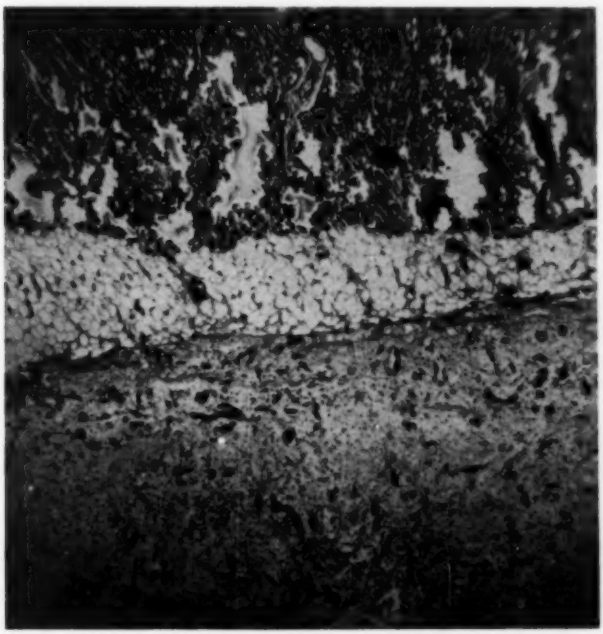

FIGURE 1: Showing fibrinous pericarditis with granulation tissue at its base, no infiltration of epicardial fat.

esophagus. The ulcer had a punched-out margin, and a smooth grey-white base.

The wall of the esophagus in this area measured 8 mm. in thickness, as compared to 3-4 mm. elsewhere.

Other pertinent pathologic findings included: Chronic passive congestion of the lungs, liver and spleen; slight bilateral straw colored pleural effusion; edema of the tracheal wall; advanced arteriosclerosis of the aorta and coronary arteries; fat replacement of the liver and chronic and acute cystitis.

Microscopic Findings: The epicardial surface of the heart was covered by wide zones of fibrin, which had been partially organized by granulation tissue at the base. The subepicardial zones contained scattered lymphocytes and histiocytes, and the epicardial fat showed no evidence of pathologic change (Figure 1).

The esophagus showed a deep ulcer, lined by granulation tissue, and below it, extensive fibrous connective tissue replacement of the esophageal wall. The wall of the esophagus and periesophageal connective tissue contained scattered collections of lymphocytes, plasma cells, histiocytes and occasional polymorphonuclear neutrophiles. The esophageal vessels here showed moderate intimal thickening by connective tissue. The uninvolved esophageal mucosa contained scattered foci of gastric glands.

Discussion

The esophagus is a hollow viscus whose walls consist of mucosa, submucosa and muscularis; it lacks the serosal coat ordinarily present in the remainder of the gastro-intestinal tract. The muscularis is surrounded by loose and dense connective tissue, which connects it with the surrounding structures.[3] The pericardial sac, however, is composed of relatively tough dense fibrous connective tissue.

It is thus understandable that an inflammatory process within the esophagus may extend into the mediastinum, without spreading into the contiguous pericardium. Despite the close proximity of the latter, the dense pericardial structure, under most circumstances, acts as an effective barrier. It is only with certain more powerful agents causing esophageal perforation that the pericardium is directly involved, and a number of instances of this kind have been reported. Foreign bodies, particularly fish and fowl bones,[4,5] as well as malignant growths of the esophagus[6] are occasionally referred to in the literature as directly causing esophageal perforation and subsequent inflammatory involvement of the pericardium.

The esophageal lesion in our case, however, was of considerable duration, the patient having complained of increasing dysphagia for approximately one year, and it is likely that sufficiently long exposure to an otherwise relatively minor trauma caused the above mentioned barrier to break down. In addition a retro-grade lymphatic spread might be considered.

The etiology of the esophageal ulcer is open to speculation. One explanation is that of ingestion of caustic liquids, a feasible possibility in view of the patient's vague alcoholic history; another, the presence of gastric type glands lining the esophageal mucosa, which may have given rise to peptic ulceration of the esophagus.[7-9]

SUMMARY

A case of fibrinous pericarditis secondary to esophageal ulceration is presented, and some of the reasons for its infrequent occurrence are discussed.

RESUMEN

Se presenta un caso de pericarditis fibrinosa secundaria a una ulceración esofágica y se discuten algunas de las razones que explican su rareza.

RESUME

L'auteur rapporte un cas de péricardite séro-fibrineuse consécutive à une ulcération de l'oesophage. Il expose les raisons de la rareté d'un tel fait.

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Editorial

PERICARDIAL HEMORRHAGE AS A HAZARD OF ANTICOAGULANT THERAPY FOR HEART DISEASE

There has been widespread acceptance of the beneficial effects of anticoagulant therapy with dicumarol during the management of the early phases of acute myocardial infarction. That this acceptance is warranted is documented by many favorable reports indicating decreased morbidity and mortality from thromboembolic disasters complicating the convalescence of patients unfortunate enough to suffer myocardial infarction. Reports from the Committee on Anticoagulants of the American Heart Association have confirmed earlier reports of improved mortality statistics for patients having myocardial infarction who received anticoagulants when compared with similar statistics for control patients.[1]

Enthusiasm has extended to the use of anticoagulant therapy for the management of congestive heart failure of other than coronary atherosclerotic etiology. In particular this adjunct has been used with well-founded logic in the management of chronic rheumatic heart disease in which there is auricular fibrillation and recurrent arterial emboli.

The major hazard of anticoagulant therapy is bleeding, and commonly cited contraindications to anticoagulant therapy with dicumarol, which include renal insufficiency, hepatic disease, ulcerative gastrointestinal disease and hemorrhagic diathesis, are well known. The need for careful and accurate supervision of therapy with determinations of prothrombin to lessen the likelihood of hemorrhage has been emphasized frequently.

Recently Goldstein and Wolff[2] have called attention to instances of pericardial hemorrhage sufficient to produce cardiac tamponade among patients who were receiving anticoagulant therapy for myocardial infarction. We also have seen a similar case in which the patient died.[3] In the cases in which necropsy was done evidence of perforation of the myocardium or of the coronary vessels was not found, but the bleeding came from capillary-laden granulation tissue in the pericardium owing to pericarditis associated with transmural infarction. Attention was called to certain diagnostic signs mentioned in the cases of Goldstein and Wolff,[2] such as undue persistence of a pericardial friction rub, recurrence of cardiac pain and signs of cardiac inflow stasis, which suggested the possibility that pericardial hemorrhage had developed.

A fatality from hematopericardium with cardiac tamponade in

a patient with nonspecific inflammatory pericarditis also has been reported. Anticoagulant therapy with dicumarol was instituted for this patient when myocardial infarction was tentatively diagnosed.[4]

In these and similar cases which are likely to come to light the unfavorable outcome must not be considered to be a toxic effect of dicumarol. A satisfactory therapeutic range of prothrombin deficiency was the rule rather than the exception and, of course, that is the aim of such treatment. This agent, however, by virtue of its profound effect on the coagulation mechanism, must be assumed to have been a factor in the bleeding from friable capillaries in granulation tissue of the pericardium traumatized by the contractions of the underlying myocardium.

The reason for avoidance of anticoagulant therapy for patients with recognized benign nonspecific pericarditis is apparent. It is evident also that treatment with dicumarol should be withheld until a definite diagnosis of myocardial infarction rather than of inflammatory pericarditis can be made based on clinical or electrocardiographic evidence. Such temporization need not seriously detract from the value of anticoagulant therapy for myocardial infarction inasmuch as the danger of complicating thromboembolism is usually not significant in the first few days after the acute attack unless the patient has profound symptoms. In the latter type of case doubt concerning the diagnosis seldom lasts long, so administration of anticoagulants can be begun promptly.

It also would appear necessary to emphasize that pericardial hemorrhage is a possible complication of myocardial infarction when patients have been treated with dicumarol so that the clinical signs can be detected early and anticoagulant-neutralizing measures promptly instituted.

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Milton W. Anderson.

Committee on Scientific Program
19th Annual Meeting

The Nineteenth Annual Meeting of the American College of Chest Physicians will be held at the Hotel New Yorker, New York City, May 28-31, 1953.

Physicians who wish to present papers at this meeting should communicate with Dr. Arthur M. Olsen, Chairman, Committee on Scientific Program, Mayo Clinic, Rochester, Minnesota.

1953 College Essay Award

The Board of Regents of the American College of Chest Physicians offers a cash prize award of two hundred fifty dollars ($250.00) to be given annually for the best original contribution, preferably by a young investigator, on any phase relating to chest disease.

The prize is open to contestants of other countries as well as those residing in the United States. The winning contribution will be selected by a board of impartial judges and the award, together with a certificate of merit, will be made at the forthcoming annual meeting of the College, to be held in New York City, May 28-31, 1953. Second and Third prize certificates will also be awarded.

All manuscripts submitted become the property of the American College of Chest Physicians and will be referred to the Editorial Board of the College journal, "Diseases of the Chest," for consideration. The College reserves the right to invite the winner to present his contribution at the annual meeting. Contestants are advised to study the format of "Diseases of the Chest" as to length, form and arrangement of illustrations, to guide them in the preparation of the manuscript.

The following conditions must be observed:

(1) Five copies of the manuscript, typewritten in English, should be submitted to the executive office, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, not later than March 15, 1953.

(2) The only means of identifications of the author or authors shall be a motto or other device on the title page, and a sealed envelope bearing the same motto on the outside, enclosing the name of the author or authors.

College Chapter News

FLORIDA CHAPTER

The Annual Meeting of the Florida Chapter was held in conjunction with the Annual Meeting of the Florida State Medical Association, April 27 at Hollywood Beach. The Chapter had its Annual Meeting with over 90 physicians in attendance.

An excellent scientific program was followed by election of the following officers:

Alexander Libow, Miami Beach, President
Nathaniel M. Levin, Miami, Vice-President
DeWitt C. Daughtry, Miami, Secretary-Treasurer
H. H. Fowler, Tampa, Program Chairman.

MICHIGAN CHAPTER

The Annual Meeting of the Michigan Chapter was held at the Detroit Tuberculosis Sanatorium on April 30. The scientific program included presentations of interesting and unusual cases and an address on the "Physiology of the Artificial Heart," by F. D. Dodrill.

The following officers were elected for the coming year:

Constantine P. Mehas, Pontiac, President
Lawrence A. Pratt, Detroit, Vice-President
Daniel W. Myers, Detroit, Secretary-Treasurer.

NEW ENGLAND STATES CHAPTER

The Monthly Meeting of the New England States Chapter and the Overholt Clinic was held on April 16 at the Deaconess Hospital, Boston, Massachusetts. Norman Wilson presented a paper entitled "Results of Pulmonary Resection in Tuberculosis."

VIRGINIA CHAPTER

The Spring Meeting of the Virginia Chapter was held at the Hotel Roanoke, May 7, Roanoke, Virginia. Many interesting papers were presented including extra-pleural pneumothorax, and iso-nicotinic acid.

Officers elected were as follows:

C. W. Scott, Burkeville, President
W. E. Roye, Richmond, Vice-President
W. E. Apperson, Richmond, Secretary-Treasurer.

WISCONSIN CHAPTER

The Wisconsin Chapter of the College will hold its Annual Meeting at the Hotel Schroeder, Milwaukee, Wisconsin, on Sunday, October 5. The following scientific program will be presented:

1:00 p.m.: *Registration.*

Scientific Exhibits.

"Pulmonary Lesions of Collagen Diseases,"
W. A. D. Anderson, J. F. Kuzma and J. L. Marks,
Marquette University Medical School.

"Uremic Pneumonitis,"
H. C. Dangle, U.S. V.A. Hospital, Wood, Wisconsin.

"Venous Catheterization of the Heart in Congenital and Rheumatic Heart Disease,"
H. L. Correll, Nathan Grossman, Armin R. Baier, Paul G. LaBissoniere, Timothy R. Murphy and Henry F. Twelmeyer,
Cardiopulmonary Division, Marquette University Medical School.

"Intermittant Positive Pressure Breathing in the Treatment of Pulmonary Emphysema,"
R. P. Jahn and F. B. Landis, U.S. V.A. Hospital, Wood, Wisconsin.

"Angiocardiography in a Case of Eisenmenger's Syndrome,"
A. Melamed and A. Marck.

"Pick's Disease with Calcification of the Pericardium,"
M. Moel, Mount Sinial Hospital, Milwaukee, Wisconsin.

"Results of Cardiac Catheterization in Patients with Pericarditis,"
Timothy R. Murphy, J. Chase and B. Nordick,
U.S. V.A. Hospital, Wood, Wisconsin.

2:00 p.m.: *Scientific Session.*

"Problems in the Diagnosis of Chest Disease,"
Herbert W. Schmidt, Rochester, Minnesota.

"Clinical Diagnosis and Treatment of Emphysema in the Patient Past Forty,"
Edwin R. Levine, Chicago, Illinois.

"Tumors of the Chest in Children,"
Gordon Ritchie, Milwaukee, Wisconsin.

"Treatment of Inoperable Cancer of the Lung,"
Edgar Mayer, New York, New York.

"Precordial Migraine,"
John F. Briggs, St. Paul, Minnesota.

6:00 p.m.: *Dinner.*

Address: "Clinical Application of Recent Advances in Cardiopulmonary Physiology,"
Aldo A. Luisada, Chicago, Illinois.

NORTHERN CHAPTER OF SOUTH AFRICA

At the Annual Meeting of the Northern Chapter of South Africa held on May 27, the following officers were elected for the coming year:

Maurine A. Pringle, Transvaal, President
Julius K. Bremer, Pretoria, Vice-President
Walter S. Linton, Transvaal, Secretary-Treasurer.

PHILIPPINE CHAPTER

The Medal of Merit of the University of Santo Tomas has been awarded to Miguel Canizares, as one of the University's most distinguished alumnus. In the 300 year existence of this university the award has been given to only four alumni.

The Quezon Institute has recently been honored by the visits of two prominent citizens of the United States, Mrs. Eleanor Roosevelt and Dr. V. M. Hoge, Assistant Surgeon General of the United States.

Presentation of the first report of the effectivity of Isoniazid in tuberculosis among 39 Filipinos was presented at the meeting of the Philippine Chapter on June 27 at the Quezon Institute. Thus study was made by Doctors Miguel Canizares, Laureano D. Bautista, Heraldo del Castillo, Carmelo P. Jacinto and Jose R. Celis, all members of the Hydrazide Committee of the Quezon Institute. An excerpt of the presidential address by Dr. Carmelo P. Jacinto follows:

"Let us review the mortality figures for tuberculosis which heads the list of death-dealing diseases in our archives. Two hundred and thirty five persons per 100,000 population (or a total of 31,987) died from it in 1931. Eight years later, in 1939—214 per 100,000 (or a total of 35,355 deaths for that year). In 1949, there were 27,815 deaths or 143 deaths per 100,000 population. There was a decrease of 40 per cent in 1949, compared to that for 1931. These figures do not include those who died from the pneumonias and the bronchopneumonias, the pulmonary

suppurations, the influenzas, the respiratory allergies, the new growths and the parasitic diseases of the respiratory organs. It is obvious, therefore, that such a group of chest workers as ours still has a great deal to accomplish in the fight against the respiratory invaders. Not only must we behave as men of science, but we must strain and strive for the widespread dissemination of medical information about chest diseases, for the elevation of undergraduate and postgraduate medical education and training in this field, and for more rigid standards of medical ethics pertaining to the practice of diseases of the chest. In short, not only must we be physicians, but preachers as well, not only doctors but educators, not only healers but crusaders."

It was reported that the Philippine Chapter now has 68 active members.

The interesting and informative scientific program was followed by election of the following officers:

Carmelo P. Jacinto, Quezon City, President
Sixto A. Francisco, Manila, President-Elect
Montano Conde, Manila, Vice-President
Laureano D. Bautista, Quezon City, Secretary-Treasurer.

College News Notes

Dr. Chevalier L. Jackson was awarded a gold medal and a certificate of merit by the Italian Federation Against Tuberculosis at a meeting arranged for him by the Italian Chapter of the College at the Carlo Forlanini Institute in Rome on June 25. Dr. Jackson presented a paper entitled, "Bronchopulmonary Segments." Dr. A. Omodei Zorini, Governor of the College for Northern Italy, presided at the meeting.

Dr. Frank R. Ferlaino was recently appointed Counselor and Advisor for the Industrial Medical Association for New York State. He was also appointed a member of the Sub-committee on Industrial Health and Accident Prevention of the Public Health and Education Committee of the Medical Society of the State of New York.

Dr. Nathaniel E. Reich, Brooklyn, New York, has recently been promoted to Clinical Assistant Professor of Medicine of the College of Medicine, State University of New York.

Announcements

A continuation course on Treatment of Diseases of the Chest will be presented by the University of Minnesota in conjunction with the American College of Chest Physicians and the Minnesota Chapter of the American Trudeau Society at the Center for Continuation Study, on October 16-18, 1952. The course is intended primarily for physicians engaged in general practice, and emphasis will be placed throughout the course on the treatment of the various types of pulmonary disease.

The Seventh Saranac Symposium will be held at Saranac Laboratory, Saranac Lake, New York, September 22-26, 1952.

A major portion of the sessions will be devoted to the latest developments in the field of pulmonary dust disease and to consider also some

of the newer forms of pneumoconiosis. The agenda will include definition of terms; ultramicroscopic dusts and pulmonary disease, the relationship between the inhalation of dust and pulmonary cancer, pulmonary disability, and the most recent aspects of compensation and medicolegal phases of pneumoconiosis.

The Department of Otolaryngology of the University of Illinois College of Medicine will hold its Annual Otolaryngologic Assembly in Chicago, September 29 to October 4. The Assembly will be divided into two parts. Part I deals with the newer concepts and development in this specialty. Part II will be concerned with anatomy and histopathology review.

The Department of Otolaryngology will also hold a special course in Broncho-esophagology, October 20 to November 1.

The University of Illinois College of Medicine will offer a combined three year residency training program in Otolaryngology, which will include the basic course material, in fulfillment of Board requirements. Residents will rotate through the Research and Educational Hospitals, the Illinois Eye and Ear Infirmary, the Hines Veterans Administration Hospital and the various affiliated institutions.

Information regarding these courses and available residencies should be made to Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

The Annual Meeting of the Eastern Section of the American Trudeau Society will be held in Philadelphia at the Bellevue-Stratford Hotel, October 31 and November 1.

Obituaries

FRANCIS E. O'BRIEN
1895-1952

Dr. Francis E. O'Brien, Fellow of the American College of Chest Physicians and former head of the Hampshire County Sanatorium, died in the Veterans Hospital, Northampton, Massachusetts on February 15, 1952, at the age of 57.

In poor health for some time, Dr. O'Brien retired from his superintendent's duty on February 1st.

Dr. O'Brien was born in Northampton, Massachusetts, on September 12, 1895. He was graduated from the Fordham School of Medicine in the class of 1917. Following graduation he enlisted in the medical corps of the United States Navy and upon his retirement in 1921, held the rank of Lt. Commander.

During World War I, Dr. O'Brien was the senior medical officer of the U.S.S. Tenadores when it was sunk off the coast of France. He was the last to leave the ship and for his heroic efforts in administering and evacuation of the wounded, he was awarded the coveted Navy Cross.

Dr. O'Brien was named superintendent of the Hampshire County Sanatorium in August, 1921. During his association as head of the sanatorium, the institution became one of the leading centers in New England for the treatment of tuberculosis. He was one of the first to recognize the value of collapse therapy in the treatment of tuberculosis.

Dr. O'Brien possessed all those great attributes of a cultured gentleman and was a source of inspirational guidance to all who knew him. He was indeed a friend to every patient who came to his sanatorium for treatment. He was a man who knew suffering and his kindly attitude in bolstering the morale of patients, their faith, their hope and consolation in their hour of need, was a responsibility which he never relinquished. His resolution to lift the tuberculosis victim of despair and apprehension was a task that he graciously undertook throughout his long and distinguished career in his chosen field.

It is not only the American College of Chest Physicians and his intimates who have suffered a loss, but Medical science itself has lost a great mind.

Dr. O'Brien was the son of the late Former Mayor of Northhampton, Massachusetts, John W. and Margaret O'Brien. He is survived by his wife, Mrs. Cecil B. O'Brien; one son, Kenneth J., assistant manager at the Veterans Administration Hospital in Iron Mountain, Michigan; one brother, James W., and three grandchildren.

Francis M. Woods, Governor for Massachusetts,
Arthur Q. Penta.

HENRY YANDELL SWAYZE
1870-1950

Dr. Henry Yandell Swayze passed away at his home in Center Point, Texas, on August 30, 1950. His death was attributed to heart failure.

Dr. Swayze was born in 1870, and was graduated from Tulane University Medical School. He practiced medicine in Mississippi and Arkansas from 1893 to 1918, when he moved to Carlsbad, Texas, to serve as superintendent of the State Tuberculosis Sanatorium for a period of time. Then he moved to Kerrville, Texas, and continued his practice, specializing in the treatment of tuberculosis. He retired from active work in 1944. A member of the American Medical Association and the Texas Medical Association, he was also a past president of the Kerr-Kendall-Gillespie-Bandera Counties Medical Society. He was a fellow of the American College of Chest Physicians. Other affiliations included the Methodist Church, Masonic Lodge and Rotary Club.

Dr. Swayze is survived by his wife and one son, Mr. P. E. Swayze, both of Center Point, Texas.

Robert B. Morrison, Governor for Texas.

RUSSELL ROBERT HENDRICKSON
1903-1951

It is with great regret that we report the death of Dr. Russell Robert Hendrickson, which occurred on December 17, 1951, in St. Francis Hospital, Crookston, Minnesota.

Dr. Hendrickson was born at Iron River, Wisconsin, August 17, 1903. He spent his childhood in Eveleth, Minnesota. In 1924, he entered the University of Minnesota Medical School, from which he was graduated in 1927. At this time Dr. Hendrickson became very much interested in the study of pulmonary disease, especially tuberculosis, and in the fol-

lowing years served as superintendent and medical director in sanatoriums in Minnesota. He went to Juneau, Alaska, in 1943, as Tuberculosis Consultant for the Territory of Alaska, and later in 1943, he went to the United States Marine Hospital, Staten Island, New York as Chief of the Tuberculosis Service. He remained there until 1945, when he returned to Minnesota and again was superintendent and medical director at sanatoriums, the last of which was Sunnyrest Sanatorium at Crookston. He was a Fellow of the American College of Chest Physicians and was a member of the Governor's Committee for Mental Health, State of Minnesota. He served as Secretary of the Clay-Becker County Medical Society from 1945 to 1949. He was a member of many honorary medical societies and civic organizations.

Dr. Hendrickson was very highly respected by the physicians in Minnesota who are especially interested in the study of pulmonary disease. He was regarded as a civic-minded and invaluable member of every community in which he resided. His loss is deeply felt by the medical profession in the state of Minnesota.

Herman J. Moersch, Governor for Minnesota.

THEODORE NEWELL RAFFERTY
1910-1951

Dr. Theodore Newell Rafferty, age 42, died April 8, 1951, after a long illness due to subacute bacterial endocarditis.

Dr. Rafferty was graduated from the University of Illinois School of Medicine in 1933. He interned at the Illinois Central Hospital in Chicago and was later on the staff of the William H. Maybury Sanatorium, located at Northville, Michigan, for three years. He was later director of the division of chest diseases at the Veterans Administration Hospital in New Orleans, Louisiana, and also lecturer in the medical department at Tulane at the same time. His last appointment, prior to his death, was as staff physician at Eastern North Carolina Sanatorium located at Wilson, North Carolina. He resigned his position due to his illness, which terminated in his death on April 8, 1951.

Dr. Rafferty, during his almost twenty years as a physician, spent almost his entire medical career in the diagnosis and treatment of pulmonary diseases—primarily tuberculosis. He was a brilliant student and was greatly admired by his associates. He was the author of a book entitled "Artificial Pneumothorax in Pulmonary Tuberculosis," published in 1944.

He is survived by his father, Dr. H. N. Rafferty, Lakeview Drive, Sebring, Florida.

Clarence M. Sharp, Governor for Florida.

MEDICAL SERVICE BUREAU

The facilities of the Medical Service Bureau of the American College of Chest Physicians are available to all who are interested in seeking positions or obtaining applicants in the field of chest diseases. If you wish to advertise in Diseases of the Chest, please write to the Medical Service Bureau, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, for rates and further information.

POSITIONS AVAILABLE

Residency available in diseases of the chest. Approved one year credit toward boards in internal medicine. Surgical training also available. Experience in all types of collapse and surgical procedures. Complete maintenance for doctor and family, situated in resort country. Must be eligible for Michigan license. Salary $4,700 to $5,700, depending upon experience. Please address Box 253A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Assistant Medical Director wanted with background in internal medicine for Mineral Springs Sanatorium, Cannon Falls, Minnesota; 100 bed county tuberculosis hospital with active medical, surgical and research program. Good salary plus furnished house. Man must be eligible for Minnesota license. Position opens January 1, 1953. Please address E. V. Bridge, M.D., Superintendent.

ANNOUNCEMENT

Postgraduate Course in Tuberculosis

Toronto Hospital for Tuberculosis, Weston, Ontario

OCTOBER 21 - 24, 1952

The National Sanitarium Association is arranging a four-day Course in Tuberculosis for physicians and surgeons. Members of the Faculty of Medicine at the University of Toronto as well as other physicians who are authorities in tuberculosis will participate in the papers to be delivered as well as in the discussions.

The Registration Fee for the Course will be $40.00 in Canadian funds payable to the National Sanitarium Association, Toronto. That amount will include attendance at all sessions at Weston and in Toronto; transportation between Toronto and Weston; three luncheons and one dinner. This fee should accompany each application.

For further information with provisional list of subjects and application form please write to: Medical Superintendent, Toronto Hospital for Tuberculosis, Weston, Ontario.

"Reduces the postoperative hospital stay by 50%"

"'*Dexedrine*' *Sulfate*, administered orally after surgery of the eye, ear, nose and throat . . . results in earlier ambulation, shortens hospitalization and hastens postoperative recovery," according to a recently published paper.[1]

Reporting on a series of 220 patients (mostly children, who were given '*Dexedrine*' in the elixir dosage form), the author states:

1. "By mid-afternoon (only 6 or 7 hours after operation) . patients were awake and active.
2. "Postnarcotic dizziness and nausea were extremely rare, and postoperative depression was reduced.
3. "Every patient was discharged from the hospital in good condition the same day with no postoperative 'hangover'.
4. "No untoward side reactions to '*Dexedrine*' were noted in any of [the] patients."

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1. Barnett, S. E.: Eye, Ear, Nose & Throat Monthly 39:19

T.M. Reg. U.S. Pat. Off. for dextro-amphetamine sulfate, S.K.F.

COLLEGE EVENTS

Intermin Session, American College of Chest Physicians, Denver, Colorado, November 30, December 1, 1952.

19th Annual Meeting, American College of Chest Physicians, Hotel New Yorker, New York, New York, May 28-31, 1953.

Wisconsin Chapter Meeting, October 5, 1952.

Chicago Postgraduate Course, October 6-10, 1952.

New York Postgraduate Course, November 10-15, 1952.

Philadelphia Postgraduate Course, March 23-27, 1953.

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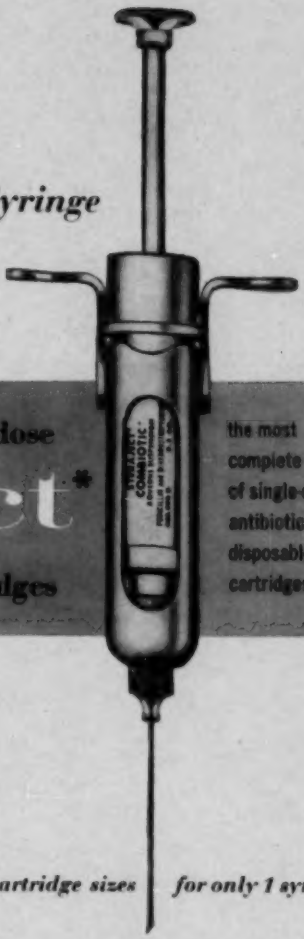

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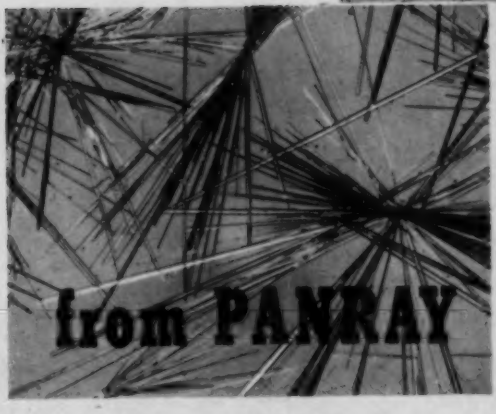

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